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VOLUME 24 NUMBER 1

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BILATERAL HYPOPLASTIC CYSTIC KIDNEYS

REPORT OF A CASE SIMULATING CHRONIC DIFFUSE NEPHRITIS IN A GIRL THREE YEARS OF AGE *

CARL H. GREENE
ROCHESTER, MINN.

Functional insufficiency of the kidney in early infancy produces characteristic clinical findings. These are best seen in cases of congenital chronic nephritis.[1] Children so affected show great developmental disturbances dating from early life, if not from birth. Associated with the developmental disturbance are stunting and backwardness in growth, difficulty in feeding, anemia and rachitis. More direct evidence of renal insufficiency is given by the excretion of a large volume of dilute urine with a low specific gravity. This urine contains a slight amount of albumin, and casts are present in small numbers. In those cases in which it has been determined, the phenolsulphonepththalein excretion is low. Death usually results from uremia. The pathologic picture in these cases is similar to, if not identical with, that seen in the chronic diffuse nephritis of adults.

The clinical findings in such cases, however, are determined by the functional rather than by the morphologic changes in the kidneys. Any renal lesion that will cause the same type of renal insufficiency will produce the same clinical changes. I wish to report a case in which the clinical symptomatology was identical with that described above, but in which the functional changes were produced by an entirely different renal lesion.

REPORT OF CASE

M. V. W. (Harriet Lane Dispensary, No. 20620), aged 3½ years, of American parentage.

Family History.—Unimportant. Third pregnancy. The second child was stillborn at full term. No history of nephritis in any of the immediate relatives.

Past History.—Spontaneous delivery at term. Birth weight, 5 pounds. The child was breast fed for only a short time and then was placed on whole cow's milk to the age of 8 months. The whole milk was then replaced by condensed milk with the addition later of a little rice and potato. The first teeth appeared

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* Received for publication, April 14, 1922.

* From the Department of Pediatrics and the Pathologic Laboratory, Johns Hopkins University, and the Harriet Lane Home of the Johns Hopkins Hospital.

[1] Greene, C. H.: Chronic Diffuse Nephritis in Childhood. Report of a Case with a Review of the Literature, Am. J. Dis. Child. **23**:183 (March) 1922.

when 1 year old. She sat alone at this time though she never walked. At the age of 8 months she is said to have had several convulsions in immediate succession, followed by stupor for the next day or two and then by pneumonia. When about 2 years old there was a similar illness accompanied by five convulsions in one day. No convulsions have followed this second attack though there was a history of irregular "spells of fever."

Examination at the first visit to the dispensary showed an underdeveloped child with a marked degree of rachitis. The urine contained a trace of albumin but no casts. The patient was treated in the dispensary for five months, during which time regulation of her diet was attempted and cod liver oil, phosphorus and bitter wine of iron were given. The weight increased, from 21 to 22 pounds, but feeding was difficult and she never ate well. She was admitted to the Harriet Lane Home August 1, with a temperature of 103 F. after having been feverish and irritable for about a week.

Physical Examination.—The patient was a markedly undernourished and underdeveloped child. Though 3½ years old the weight was only 22 pounds (average weight for age 33.5 pounds). Anemia was marked and the skin presented a uniform ivory-like pallor. The child was rachitic with extreme deformity of the head, chest and extremities. Muscular development was poor although she was able to sit up unsupported. No effort was made to stand or walk and the tibial bowing would have rendered the feat difficult. She talked with a fair degree of distinctness and there was no apparent mental retardation.

Head: Typically rachitic in shape, large and square with pronounced frontal and parietal bosses. The anterior fontanel was open admitting one finger tip. The eyes and ears were normal. The throat showed slight injection of the pharynx and hypertrophy of the tonsils. The lips and mucous membranes were anemic.

Chest: Markedly rachitic in type with great flattening of the sides and a nearly rectangular cross section. Harrison's groove was prominent and was further accentuated by the flaring of the lower ribs. A distinct rosary was present. Respirations were quiet; abdominal in type.

Lungs: Clear on percussion and auscultation.

Heart: The relative cardiac dullness measured 1 by 6.5 cm. at the fifth interspace with the point of maximum impulse 6 cm. from the midsternal line. The heart sounds were clear and the aortic second sound was not accentuated. The pulse was regular in rate and rhythm and of good quality.

Abdomen: Large and distended. The muscle tone was poor. No fluid could be made out. The liver was enlarged, extending 4 cm. below the costal margin. The edge was smooth and sharp. The spleen was greatly enlarged, measuring 6 by 10 cm. and extending from the twelfth rib behind nearly to the iliac crest and a third of the way to the umbilicus anteriorly. The kidneys were not palpable.

Extremities: Marked distortion of all the long bones was present. The humeri appeared relatively short owing to bowing. The radius was nearly 1 cm. longer than the ulna, leaving the hand in a position of extreme adduction. The femora also showed bowing. The lower third of the tibia was bent posteriorly through an angle of nearly 90 degrees leaving the long axis of the foot in a plane parallel to the axis of the leg. Muscular weakness was marked.

Tendon reflexes: Present and equal on both sides though they were very feeble.

Laboratory Reports.—Blood examination: Leukocytes, 13,350; erythrocytes, 2,460,000; hemoglobin (Sahli), 43 per cent. Differential count: Polymorphonuclear neutrophils, 35 per cent.; polymorphonuclear eosinophils, 6 per cent.; polymorphonuclear basophils, none; lymphocytes, 33 per cent.; pathologic lymphocytes, 9 per cent.; large mononuclears, 3 per cent.; transitionals, 6 per cent.; myelocytes, 1 per cent.; myeloblasts, 2 per cent.; unclassified, 5 per cent. The red cells were pale with some poikilocytosis and rather marked anisocytosis. The platelets were diminished in number. The blood picture was that of a severe secondary anemia with a moderate degree of bone marrow stimulation.

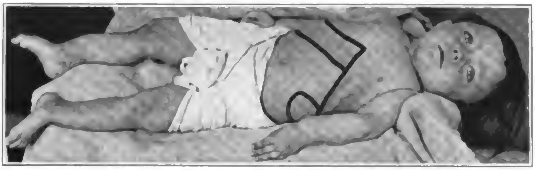

Fig. 1.—Photograph of the patient. The costal margins and the edge of the liver and spleen are outlined.

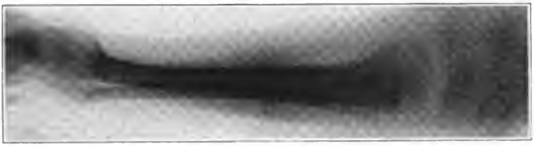

Fig. 2.—Roentgenogram of the leg showing the bowing of the tibia and the rachitic changes at the ankle and knee.

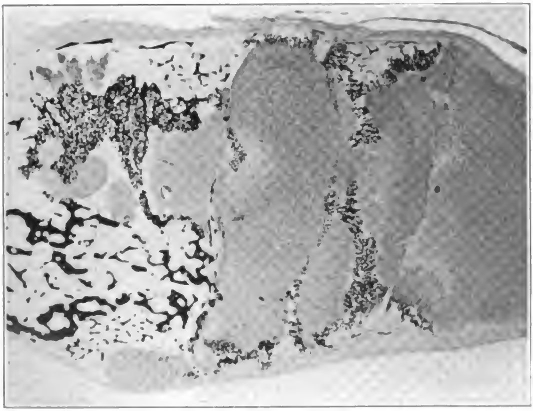

Fig. 3.—Section through the costochondral junction showing the extensive rachitic changes. Three distinct lines of healing. Stained with silver to show the calcium phosphate deposits.

Urine: Pale yellow, faintly acid. Specific gravity, 1.009. Albumin (Esbach), 1.5 gm. per liter. A trace of acetone was present. No sugar, bile or blood. Microscopic examination showed many epithelial cells, a few pus cells but no casts.

Phenolsulphonephthalein excretion in two hours was 7 per cent.

Total urine: Twenty-four hour specimen of urine showed some polyuria and a distinct tendency toward fixation of the specific gravity and nitrogen concentration. Day urine, 9 a. m. to 9 p. m.: 400 c.c., specific gravity, 1.009; nitrogen, 0.22 per cent. Night urine, 9 p. m. to 9 a. m.: 260 c.c.; specific gravity, 1.011; nitrogen, 0.22 per cent. Total urine in twenty-four hours: 660 c.c.; specific gravity, 1.010; nitrogen, 0.22 per cent.

Wassermann and tuberculin reactions were negative.

Course in Hospital.—The temperature returned to normal soon after admission but food was refused or only taken poorly. In addition to the polyuria, polydipsia and pollakiuria were marked. A repetition of the phenolsulphonephthalein test on a catheterized specimen gave a 4 per cent. return.

There was no marked change in the general condition until August 6, when the child became very much weaker, developed hyperpnea and became stuporous. Respirations were slow, labored and stertorous. The pulse was weak and feeble with a marked pulsus alternans. The maximum systolic blood pressure varied between 100 and 108 with nearly 20 mm. difference in the systolic pressure of alternate beats. The diastolic blood pressure was between 65 and 70. The carbon dioxid capacity of the blood at this time was 18 volumes per cent. and the nonprotein nitrogen was 48 mg. per 100 c.c. Examination of the eye grounds revealed slight diffuse congestion, but no suggestion of albuminuric retinitis. Sodium bicarbonate was given by mouth in large doses with gradual improvement. The following day the carbon dioxid capacity of the blood had increased to 26 volumes per cent. Two days later the hyperpnea ceased though the urine continued to show large quantities of acetone and diacetic acid. Five days later (August 13) the patient had apparently recovered and was in fairly good condition. She was brighter and more alert and able to take her feedings well.

There was very little change in the general blood picture. Leukocytes, 17,500; erythrocytes, 2,590,000; hemoglobin (Sahli), 41 per cent.

Urine: A clear, lemon yellow, acid specimen. Specific gravity, 1.012. Albumin (Esbach) 1.75 gm. per liter. No acetone or diacetic acid present.

Phenolsulphonephthalein excretion in two hours was 6 per cent.

Carbon dioxid capacity of the blood was 35 volumes per cent. Blood pressure: systolic, 96; diastolic, 60; with no alterations of the pulse.

At this time a cystoscopic examination was made. Abdominal palpation under anesthesia was apparently negative, as neither kidneys nor ureters could be palpated, though the liver, spleen and pancreas were easily felt. Cystoscopic examination showed a normal bladder. Urine cultures were negative.

Owing to the poor condition of the patient (the weight had fallen to 18 pounds) and the increasing anemia, transfusion was determined on. August 16, the child was given 175 c.c. of citrated whole blood from the father. There was no reaction following the transfusion other than a slight rise in temperature. Improvement in the appetite and general condition was marked. Four days after transfusion the carbon dioxid capacity of the blood was 41 volumes per cent.

Blood examination: Leukocytes, 9,000; erythrocytes, 3,560,000; hemoglobin (Sahli), 60 per cent. Differential count: Polymorphonuclear neutrophils, 26 per cent.; polymorphonuclear eosinophils, 4 per cent.; polymorphonuclear basophils, 5 per cent.; lymphocytes, 37 per cent.; pathologic lymphocytes, 8 per cent.; large mononuclears, 1 per cent.; transitionals, 5 per cent.; myelocytes, none; myeloblasts, 1 per cent.; unclassified, 13 per cent. The red cells were essentially normal. There were many poorly stained and fragile forms of leukocytes difficult of interpretation, but they were probably mostly lymphocytes.

Urine: Slightly cloudy, pale yellow specimen, acid. Specific gravity, 1.012. Albumin (Esbach), 0.75 gm. per liter. No acetone or diacetic acid. Epithelial and a few pus cells were present but no casts.

Phenolsulphonephthalein: The two hour excretion was 8 per cent.

The child continued to improve rapidly. She ate fairly well, but continued to be particular as to her diet, refusing eggs, though taking bread and milk, and gaining in weight. She was bright and alert. The pollakiuria became less marked but total samples were not saved so that we are unable to state whether this change was due to a lessening of the degree of polyuria or rather to lessened bladder irritability. Blood examination, September 1: Leukocytes, 14,000; erythrocytes, 2,960,000; hemoglobin (Sahli), 70 per cent. There was no change in the differential count. The red cells were dark with some diffuse basophilia. Platelets were still diminished. Four normoblasts were seen.

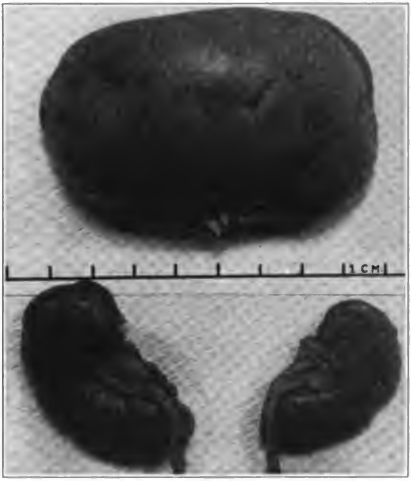

Fig. 4.—The two kidneys compared with a normal kidney from a child of the same age.

Urine: Pale yellow specimen, acid; specific gravity, 1.013. Albumin (Esbach), 0.75 gm. per liter. No acetone or diacetic acid. No casts or pus cells.

Phenolsulphonephthalein: The two hour excretion was 10 per cent.

The patient's condition at this time was sufficiently satisfactory to warrant her discharge from the hospital. Weight, 20 pounds 6 ounces.

She proved to be difficult to manage at home. Her appetite became progressively poor and capricious so that finally she refused all food other than milk, rice and potatoes. She was given reduced iron, but the hemoglobin fell rapidly. She developed a cough and began to lose weight and was readmitted to the Harriet Lane Home, September 26.

Examination at this time showed evidences of a severe anemia and recent loss of weight. There was a slight rhinopharyngitis. The patient's condition otherwise was the same as on her first admission to the hospital. The measurements of the liver and spleen were identical with the earlier ones. The systolic blood pressure was 102, the diastolic, 68.

Blood examination, September 26: Leukocytes, 13,900; erythrocytes, 2,496,000; hemoglobin (Sahli), 28 per cent.

Urine: Pale yellow specimen, acid; specific gravity, 1.011. Albumin positive. No acetone or diacetic acid. A few epithelial and white blood cells were present but no casts or red blood cells.

Phenolsulphonephthalein. The two hour excretion was 7 per cent.

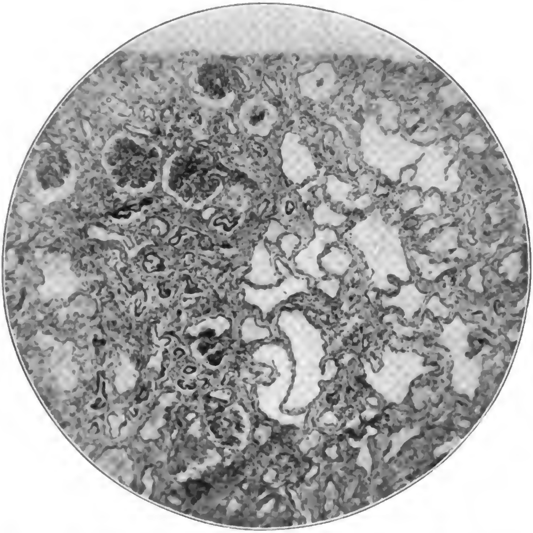

Fig. 5.—Cortex of the kidney showing the large peripherally situated glomeruli and the enormously dilated tubules.

The patient continued to present a difficult feeding problem during the remainder of her hospital course. She persistently refused all food but milk, rice and potatoes though she could be forced to eat small amounts of egg, scraped beef and vegetables.

An Ewald breakfast October 12 revealed the presence of an hypochlorhydria. Removed at one hour it showed free hydrochloric acid, none; combined acid, 24; hydrochloric acid deficit, 40.

Dilute hydrochloric acid was then given in the hope that the appetite might be improved, but unavailingly. The child continued rapidly to lose weight.

Slight hyperpnea was observed October 18 and the carbon dioxid capacity of the blood was found to be 19 volumes per cent. The hydrochloric acid was then discontinued and sodium bicarbonate substituted.

October 24, the child's condition underwent a distinct change for the worse, associated with a progressively rising temperature and a rapid loss of weight. Vomiting made it necessary to stop all feedings and administer fluids by means of the rectal drip method. Anuria developed October 27. The temperature remained in the neighborhood of 103 F. and death ensued on the following day.

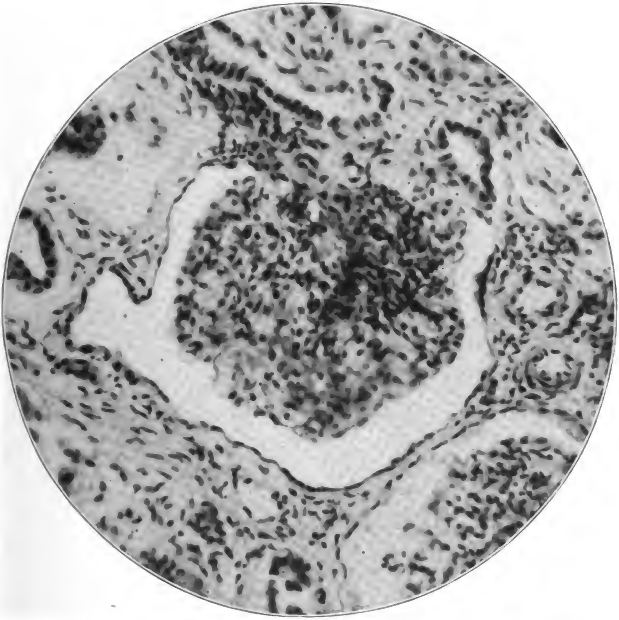

Fig. 6.—Glomerulus showing the dilatation of Bowman's capsule and the round cell infiltration through the section.

Macroscopic Findings (No. 6038).[2]—Body: The body was that of a small child greatly undersized for her age. The skin showed an extreme pallor and there were marked rachitic deformities present, accompanied by muscular atrophy. The long bones of both arms and legs showed epiphyseal enlargements and symmetrical bowing of the shafts, especially the tibias. Saber-shin and toe-drop deformities were present. The axillary and cervical lymph glands were easily palpable.

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[2] I am indebted to Dr. J. Paul of the Department of Pathology for permission to report the necropsy findings.

On opening the peritoneal cavity the abdominal viscera appeared to be unusually pale. The serous surfaces were smooth and the cavity contained no fluid. The viscera were normally disposed but the liver, slightly enlarged, projected 1.5 cm. below the costal margin and the inferior end of an enlarged spleen was visible. Prominent and numerous lymph glands appeared in the mesentery.

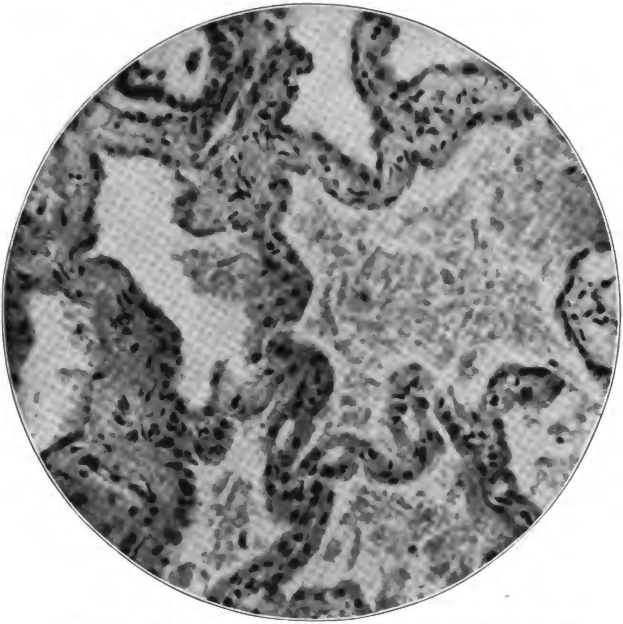

Fig. 7.—Dilated and cystlike tubule showing the flattened epithelium, the communication between the different cysts, and the cellular débris filling the tubules.

The thoracic cavity was narrow and compressed and the enlargements of the costochondral junctions stood out on its external surface and projected into the pleural cavities as nodules on the anterior thoracic wall. The heart

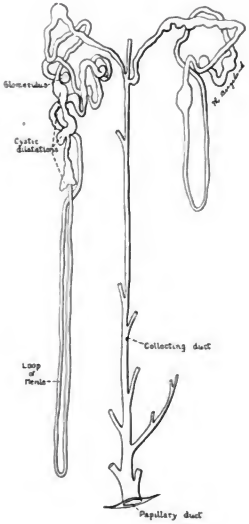

Fig. 8

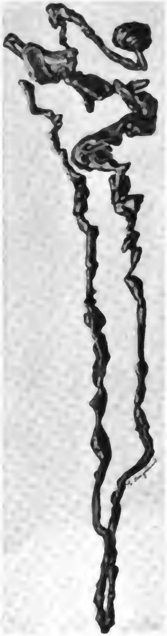

Fig. 9

Fig. 8.—Semidiagrammatic sketch to show the general relationship of the renal tubules and the cystic dilatations. Made from a dissection of the tubules by Dr. H. F. Traut.

Fig. 9.—Wax reconstruction of a dilated tubule to show the character of the cystic dilatations. The glomerulus, the proximal convoluted tubule, the loop of Henle and the beginning of the distal convoluted tubule are shown.

occupied the major portion of the lower thorax, its apex lying close to the left thoracic wall while the lower lobe of the left lung was practically entirely anterior to it.

Heart: No hypertrophy of the heart was present; it was small, weighing only 50 gm. Both epicardium and endocardium were smooth. The valves were delicate and apparently competent. The myocardium appeared to be normal.

Lungs: Both lungs were small and almost white in color, their consistency being everywhere soft and cushiony. The pleural surfaces showed an unusual degree of wrinkling. They were pale and somewhat opaque in appearance. On section the cut surface showed slightly atelectatic lung tissue.

Spleen: The spleen was of unusual appearance. It was large, weighing 100 gm. and measuring 9.5 by 4.5 by 2.5 cm. It was dark purple in color and very firm in consistency. It was tense and smooth. On section the splenic pulp was dark red and firm. Many prominent, but small, greyish malpighian bodies were visible.

Mesenteric lymph glands: These glands, averaging 0.5 cm. in length, appeared in great numbers throughout the proximal portions of the mesentery.

Liver: The liver was large, weighing 500 gm. and measuring 13.5 by 7.5 by 7 cm. Its color was pale brown, in keeping with the pallor of the other organs. It was somewhat mottled and many small fatty areas were present. These were light in color and diffuse in distribution, appearing both on the surface and on section.

Suprarenals: These organs showed no gross abnormalities.

Kidneys: The picture presented by the kidneys was most unusual. Both organs were atrophic, the right more so than the left. The left kidney weighed only 10 gm. and its dimensions were 5 by 3 by 1.5 cm. It was pale grayish red. The surface was quite smooth, the capsule stripped with ease and practically no signs of fetal lobulations were present. On section, the renal pelvis appeared relatively large, considering the small size of the organ. Distortion of the normal kidney architecture was present, and the cortex was very thin and ill defined, measuring about 2 or 3 mm. in width. In its place and in the columns of Bertini and in the distal portions of the medulla the tissue appeared as a fine, loose meshwork, composed of irregularly dilated tubules or innumerable small irregular cysts. The cortical striations were masked by this picture. Throughout the medulla an increase in fibrous tissue was present.

The right kidney was smaller, weighing only 7 gm., and measuring 4 by 2.5 by 1.5 cm. It was similar in appearance to the left. The cortex was again ill defined and almost microscopic.

Both ureters showed some dilatation, the one on the left being slightly larger than the right. No demonstrable ureteral strictures were present.

Bladder: Contained a few cubic centimeters of very cloudy urine. The mucous surface of the bladder was normal but very pale. Over the trigone there were numerous submucous hemorrhages. Hemolytic streptococci, staphylococci and colon bacilli were grown from a urine culture taken at the time of necropsy.

Intestines: Peyer's patches were prominent, especially in the region of the ileocecal valve.

Bones: Great enlargement, as described above, of the costochondral junctions was present. This was especially noticeable from the third to the eighth rib. On section the line of demarcation between cartilage and bone was thick and irregular.

Bone marrow: The marrow from the right femur was unusually hyperplastic. It had the appearance of dark red jelly.

Brain: The brain did not show any gross abnormalities.

Microscopic Findings.—Heart: Sections show normal heart musculature.

Lungs: A considerable degree of atelectasis was present with compression and thickening of the alveolar walls. There was also an excess of peribronchial fibrosis. A heavy, thick, subpleural layer of fibrous tissue was present and the pleura was elevated into folds which lay lengthwise along the lung surface, compressing the tissue beneath them. There had been metaplasis of the lining cells of the pleura, and instead of the usual flattened serosal cells, the pleura was composed of high columnar cells with distally placed nuclei.

Spleen: There was a noticeable decrease in fibrous trabeculae and a great predominance of endothelial cellular elements present in the splenic pulp. The malpighian corpuscles were prominent, numerous, and showed pale centers filled with large vesicular cells, but with a peripheral ring of dark, small round cells. Throughout the splenic pulp a great number of red blood corpuscles were seen and normoblasts were undoubtedly present.

Liver: The section presented a uniform appearance, but the portal spaces were abnormally distinct, showing an increase in fibrosis and the presence of small round cells and fibroblasts in close association with the bile ducts, a peribiliary reaction. Surrounding these portal spaces there was pronounced vacuolization of the liver cells and peripheral degeneration of the lobules. Signs of a hematogenous function were present, for many of the sinusoids distributed evenly throughout the section contained a few small cells with dark, pyknotic nuclei resembling groups of normoblasts seen in the liver of newly born or premature children.

Suprarenals: Sections of the suprarenals did not show any abnormality.

Kidneys: The microscopic picture will be discussed later.

Bladder: Two sections through the bladder wall, one taken from the region of the trigone and one from the fundus, appeared normal and showed little or no histologic evidence of cystitis.

Costochondral junctions:[3] The rachitic deformities were extreme. The changes in the bones as revealed by both the roentgen-ray and histological examination were most extensive. They differed, moreover, from the changes ordinarily found in rachitis. The proliferative cartilage was most irregular and the calcification was defective. In the deep metaphysis were large islands of cartilage bordered on one or more sides by dense calcium deposits. These islands of cartilage gave the metaphysis, as seen in the roentgenogram, a honeycomb appearance. The trabeculae were thin and the osteoid borders, comparatively speaking, narrow. Surrounding the trabeculae and islands of cartilage and lying between them was loose fibrous tissue. Obviously, for a long time the pathologic condition in the bones had been in a state of flux between healing and relapse.

Bone marrow: A smear taken at the time of necropsy and stained with Wright's stain showed many well-formed red blood cells which varied considerably in size. The number of nucleated forms appeared to be normal; normoblasts markedly predominating. There was no basophilia. The number of white blood cells present was normal. Some myelocytes and an occasional myeloblast were present. Many undifferentiated mononuclear cells with finely reticulated, purplish staining, nuclei were seen. These were the normal, undifferentiated bone marrow cells.

Sections stained with both hemotoxylin and eosin and Wright's stain showed a very hyperplastic marrow. The predominating cells showed large vesicular nuclei, and could not be classified other than as undifferentiated bone marrow cells. Great numbers of early cells of the granular series were present and they predominated over the early red cells. Normoblasts were frequent, but only an occasional megaloblast was seen. Great numbers of large megakaryocytes were seen scattered through the marrow.

DISCUSSION OF CLINICAL FINDINGS

Clinically, the findings in this case were those of a long standing renal insufficiency and were identical with those seen in the cases of typical chronic interstitial nephritis. In this case the family history was negative. The condition was present from birth but symptoms of renal disturbance first appeared at the age of 8 months. At this time the child had convulsions that probably marked the first of a series of uremic attacks.

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[3] I am indebted to Dr. E. A. Park for the discussion of the changes in the bones.

Following the convulsions, the patient was put on a faulty diet and evidences of rachitis followed. The character of the diet was due, in part, to the ignorance of the parents, but in even greater measure it was due to the idiosyncrasies of the patient. Difficulty in feeding was always present and during her stay in the hospital the child would eat only milk, rice and potato unless forced to take other things. Similar cases have been reported by Oppenheim [4] and Paterson [5] among others. It is not surprising that an extreme degree of rachitis should develop on such a diet.[6] It must be recognized, however, that other factors [7] may have entered into the development of the rachitis in this child.[8] A marked degree of renal insufficiency was also present.

Blood smears taken in this case showed a pronounced secondary anemia. Similar blood changes are found in many cases of rachitis but the type of anemia found in infants is not specific in character [9] and the anemia in this child may have been due, in part, to the renal insufficiency as well as to the rachitis. The remarkable clinical improvement following a single transfusion is of interest. This is especially so since there apparently was no great stimulation of the hemopoietic system. The increase in the erythrocyte count lasted for about a month which corresponds well with the average life of the transfused blood corpuscle.[10] During this period there was a great improvement in the general condition of the patient and even a slight increase in the phenolsulphonephthalein output, indicating that the kidneys were functionally benefited by the general improvement.

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[4] Oppenheim, A.: Ueber Schrumpfniere im Kindesalter, Inaug. Dissert. Halle, 1891.

[5] Paterson, D. H.: Three Cases of Renal Dwarfism Associated with Curious Bony Changes, Proc. Roy. Soc. Med. **13**: Sec. Dis. Child., 107, 1920.

[6] The recent work of McCollum, Simmonds, Shipley and Park [7] has indicated that rachitis may be caused by a disturbance in the balance of inorganic salts in the diet when combined with an insufficiency of an organic factor. Disturbance of the calcium-phosphate ratio was more effective in producing rachitic changes than was the absolute amount of these salts present in the diet. Phosphate retention is known to be an accompaniment of nephritic acidosis. It would seem, therefore, that if renal insufficiency were to disturb the calcium-phosphate balance in the blood of a growing child, rachitis might result. Unfortunately, accurate blood studies were not possible in the present instance, and we are unable to present, at the present time, the experimental data requisite to prove this hypothesis. The problem of "renal rickets" has recently been discussed in detail by Shipley, Park, McCollum and Simmonds.[8]

[7] McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: Studies in Experimental Rickets. VIII. The Production of Rickets by Diets Low in Phosphorus and Fat-Soluble A, J. Biol. Chem. **47**:507, 1921.

[8] Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, W.: Is There More Than One Kind of Rickets? Am. J. Dis. Child. **22**:91 (July) 1922.

[9] Evans, F. A., and Happ, W. M.: Secondary Anemia of Infants. A Study of the So-Called Infantile Splenic Anemia or Anemia Infantum Pseudoleukemica, Johns Hopkins Hosp. Bull. **33**:1, 1922.

The functional efficiency of the kidneys in this child was low. Increased frequency of urination had been noticed at home. In the hospital a moderate increase in the fluid intake and output was noted. The specific gravity of the urine was low, the limits of variation being from 1.005 to 1.012. A fixation test was not done, but on comparing the total day and night urines there was a definite suggestion of a fixation of the specific gravity and an inability to concentrate the nitrogenous excreta. As in the case of Paterson the phenolsulphonephthalein excretion was extremely low.

Albumin was present in the urine throughout the whole period of the disease. The amount was increased during the uremic attacks, but was never large. No Bence-Jones or protein body other than serum protein was demonstrable in the urine. Casts were absent even during the terminal stages of the disease.

The blood chemistry has not previously been reported on in this type of case and it is to be regretted that complete blood analysis was not possible. The nonprotein nitrogen was 48 mg. per 100 c.c., a value which may be compared with the figures of Schlutz and Pettibone [11] of from 23 to 40 mg. in the blood of new born infants, of Tileston and Comfort [12] of from 20 to 34 mg., of Leopold and Bernhard [13] of from 19 to 40 mg. in the blood of normal children, and of Leopold and Bernhard [13] of from 34 to 52 mg. in miscellaneous cases of chronic nephritis in childhood. It is apparent that there was a definite nitrogenous retention in the blood even though the type of this retention could not be determined.

The systolic blood pressure was 108 and the diastolic 70. While this may indicate a slight hypertension for a child aged 3½ years, it is not marked. There were no evidences of cardiovascular changes.

Death was due to uremia, though starvation acidosis undoubtedly was a contributing factor.

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[10] Ashby, W.: Determination of Length of Life of Transfused Blood Corpuscles in Man, J. Exper. Med. **29**:267, 1919.

[11] Schlutz, F. W., and Pettibone, C. J. V.: Quantitative Determinations of Nonprotein Nitrogen in the Blood of the New-Born, Am. J. Dis. Child. **10**:206 (Sept.) 1915.

[12] Tileston, W., and Comfort, C. W.: The Total Nonprotein Nitrogen and Urea of the Blood and the Phenolsulphonephthalein Excretion in Children, Am. J. Dis. Child. **10**:278 (Sept.) 1915.

[13] Leopold, J. S., and Bernhard, L.: The Nonprotein Nitrogenous Constituents of the Blood and the Phenolsulphonephthalein Test in Children, Am. J. Dis. Child. **11**:432 (June) 1916.

DISCUSSION OF THE PATHOLOGIC FINDINGS

The resemblance between the clinical findings in this case and those of chronic diffuse nephritis was marked. The clinical findings in both types of cases were determined by the extreme impairment of renal function but the kidney lesions were very different anatomically.

In the majority of cases considered in a previous paper[1] the pathologic findings in the kidney were similar to those found in the primary diffuse nephritis of adults. In the present case, the kidneys present a different pathologic picture. The sections were remarkable because of the marked dilatation of the tubules. This dilatation was general but was most marked in the peripheral half of the organ. In this peripheral zone the convoluted tubules assumed enormous proportions. They appeared as large, irregular, open spaces lined with epithelium, essentially cuboidal in type, and in a fair state of preservation. In these areas of tubular dilatation the interstitial tissue was practically insignificant and a picture not unlike lung tissue was formed. Most of the spaces contained coagulated fluid but a few cellular casts were seen. In the cortex the glomeruli showed great increase in size. The majority of the largest ones appeared close to the capsule of the kidney, but the glomerular hypertrophy was general. Signs of chronic inflammation, for the most part interstitial in character, were present throughout the entire section. It was most prominent close to the capsule where there was a peripheral zone of marked round cell infiltration and fibrosis. The glomeruli themselves escaped direct involvement other than thickening of the capsule of Bowman. Through the zone of dilatation this inflammatory reaction was not marked, but in the region of the papillae there again was diffuse, round cell infiltration, and some interstitial fibrosis. Some of the papillary tubules showed epithelial proliferation. A few of them contained red blood cells but other signs of an acute nephritis were lacking.

The appearance of the zone of dilated tubules suggested that this was a case of early congenital cystic kidney. Congenital cystic kidney is found under widely varying circumstances and an extensive literature has arisen concerning the mode of origin of the cysts. Numerous theories have been proposed to explain the development of the polycystic kidney but at present only two are seriously accepted: (1) the theory that the process is due to a neoplasm; (2) the theory that the process is due to congenital malformation. Various combinations of these two theories have also been proposed.

The older theory of Virchow[14] has been discarded completely. He assumed that the cysts in congenital cystic kidney were retention cysts of inflammatory origin. Following an intrauterine papillitis or nephritis, the proliferation of scar tissue caused an obliteration of the collecting tubules with resultant cyst formation. Busse [15] and Berner,[16] in particular, have pointed out that the proliferation of the interstitial tissue is secondary to the cystic changes. In addition, Petterson [17] produced an experimental obliteration of the collecting tubules in rabbits by ligating the renal papilla. This resulted in a temporary dilatation of the entire tubule followed by atrophy. Tollens [18] found similar atrophy and destruction of the tubules following cauterization of the papilla.

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[14] Virchow, R.: Ueber congenitale Nierenwassersucht, Ges. Abhandl. z. Wissench. Med. Frankfurt, 1856, p. 864.

Brigidi and Severi [19] first brought the theory of new growth into prominence. They observed epithelial proliferation in the tubules and the formation of epithelial nests which became converted into cysts by secondary degenerative changes. Papillary outgrowths from the epithelium of the dilated tubules were also observed. The changes in the kidney showed marked similarity to those occurring in cystadenomas of the ovary. Because of this the renal lesion was classified as a true neoplasm. Nauwerck and Hufschmid [20] emphasized the evidence of new growth associated with congenital cystic kidney. They recognized buds from the tubules, intracystic papillary growths, and the development of epithelial cell nests. With Von Kahlden [21] they emphasized the frequent association of cystic changes in the liver with cysts in the kidney. Von Kahlden, in particular, thought the changes in the liver were due to the adenoma or cystadenoma of the bile passage and the association of this condition with similar changes in the kidney spoke very strongly for the identity of the pathologic process involved in both instances.

In two cases of congenital cystic kidneys and liver occurring in infants Bunting [22] showed that there was a condition of hyperplasia of the duct epithelium with a tendency to cyst formation. This was most marked in the kidneys and liver but occurred to a less degree in the pancreas. Bunting found some increase in the number of tubules but there was no sharp distinction between abnormal tubules and normal renal parenchyma. The evidence of epithelial hyperplasia was widespread, and Bunting did not think the diagnosis of adenocystoma justified. The familial character of his two cases lead him to a diagnosis of congenital malformation rather than of neoplasm.

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[15] 15. Busse, O.: Ueber Cystenniere und andere Entwicklungsstörungen der Niere, Arch. f. path. Anat. u. Physiol. **175**:442, 1904.

[16] 16. Berner, O.: Zur Zystennierenfrage, Arch. f. path. Anat. u. Physiol. **211**: 265, 1913.

[17] 17. Petterson, A.: Ueber die Veränderungen der Niere nach Läsion der Papille beim Kaninchen. Beitr. z. path. Anat. u. z. allg. Path. **33**:606, 1903.

[18] 18. Tollens: Ueber die Folgen der Markkegelobliteration der Kaninchenniere, Arch. f. path. Anat. u. Physiol. **177**:477, 1904.

[19] 19. Brigidi, V., and Severi, A.: Contributo alla pathogensi delle cisti renale, Lo Sperimentale **46**:1, 1880.

[20] 20. Nauwerck, C., and Hufschmid, K.: Ueber das multiloculare Adenokystom der Niere. Ein Beitrag zur Kenntniss der Cystenniere, Beitr. z. path. Anat. u. z. allg. Path. **12**:1, 1893.

[21] 21. Von Kahlden, C.: Ueber die Genese der multiloculären Cystenniere und der Cystenleber, Beitr. z. path. Anat. u. z. allg. Path. **13**:291, 1893.

[22] 22. Bunting, C. H.: Congenital Cystic Kidney and Liver with Family Tendency, J. Exper. M. **8**:271, 1906.

The familial and hereditary occurrence of congenital cystic kidney has been noted by many authors since the time of Virchow. Not only are congenital cystic kidneys frequently familial in origin but a long series of associated congenital malformations have been reported. Dunger [23] and Meyer [24] have both reviewed this literature in detail.

The explanation of the mechanism for the origin of congenital cystic kidney as a congenital malformation have varied greatly with the conception of the normal development of the kidney current at the time. Hildebrand [25] made use of the modern dualistic theory [26] of the formation of the permanent kidney. He postulated a failure of union between the collecting and convoluted tubules. The cysts were assumed to be retention cysts developing in the glomeruli and convoluted tubules. Ribber [27] assumed the same type of developmental defect of the tubules but emphasized the importance of proliferative changes in the epithelium in their relation to cyst formation. This explanation of the mechanism of cyst formation has received much support from the reconstructions of the tubules from cases of congenital cystic kidney made by Meader [28] and Forssman.[29]

Meader found glomeruli without uriniferous tubules, glomeruli with dilated capsules but no outlets, and glomeruli opening into short uriniferous tubules which ended in cysts. Study made clear that the glomerulus and the proximal portion of the uriniferous tubule were the parts involved in his case, but Meader did not feel justified in drawing conclusions as to the mechanism responsible for the lesion. Forssmann agreed with Hildebrand in thinking that the cysts were retention cysts. The proliferative changes in the epithelium are striking in many instances and Staemmler [30] among others, admits the developmental defect in the tubule but insists that the secondary changes are neoplastic in character. McKinley [31] has recently reviewed the subject of the epithelial changes in cystic kidney. He emphasized the similarity of the changes to those seen in compensatory hyperplasia of the kidney from other causes and suggested that the changes in the epithelium were expressions of compensatory effort in an organ whose functional capacity had been reduced by primary cystic changes.

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[23] Dunger, R.: Zur Lehre von der Cystenniere mit besonderer Berücksichtigung ihre Heredität, Beitr. z. path. Anat. u. z. allg. Path. **35**:445, 1904.

[24] Meyer, E.: Ueber die Entwicklungstörungen der Niere, Arch. f. path. Anat. u. Physiol. **173**:209, 1903.

[25] Hildebrand, O.: Weiterer Beitrag zur pathologischen Anatomie der Nierengeschwülste, Arch. f. klin. Chir. **48**:343, 1894.

[26] Felix, W.: The Development of the Urinogenital Organs, Manual of Human Embryology (Keibel and Mall), Philadelphia **2**:752, 1912.

[27] Ribbert, H.: Ueber die Entwicklung der bleibenden Niere und die Enststehung der Cystienniere, Verhandl. d. deutsch. path. Gesellsch. **2**:187, 1900.

[28] Meader, F. M.: A Study of the Anatomical Relations in a Congenital Cystic Kidney, Johns Hopkins Hosp. Bull. **18**:353, 1907.

[29] Forssman, J.: Rekonstruktionen von Cystennieren, zugleich ein Beitrag zur Kenntnis der Entstehung von Cystennieren, Beitr. z. path. Anat. u. z. allg. Path. **56**:500, 1912.

Failure of union of the two separate elements of the renal anlage will not explain the origin of all cases of cystic kidney. Von Mutach [32] and Bunting,[22] by a study of serial sections, were able to prove the continuity of the renal tubules in the cases reported by them. Berner [33] also found carmine in the cysts after its injection into the ureter. In all of these cases well developed cysts were present. Retention alone will not suffice to explain the origin of the cysts.

In order to study the true pathologic picture in the present case, the kidney tubules were modeled by the well known wax plate reconstruction method. Distortion of the sections by the dilatation of the tubules made reconstruction difficult but it was usually possible to follow any tubule through part of its course and several were followed through greater distances. The kidney was also studied by digestion in hydrochloric acid and dissection of the individual tubules.[34]

The glomeruli were large and showed very little change although the tuft seemed to be somewhat looser and less compact than normal and the glomerular capsule was slightly distended. The changes in the tubules varied slightly in the different parts of the kidney but, in general, the first portion of the proximal convoluted tubule was only slightly dilated. Its epithelium was cuboidal and somewhat swollen and granular. The changes in the tubule first became striking in the second portion of the proximal convoluted tubule. This portion of the tubule was distorted out of all recognition by a series of large cystic dilatations. For the most part these dilatations approached the spherical although some were fusiform in shape. The epithelium of these cysts was primarily cuboidal although in many places it was

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30. Staemmler, M.: Ein Beitrag zur Lehre von der Cystenniere, Beitr. z. path. Anat. u. z. allg. Path. **68**:22, 1921.

31. McKinlay, C. A.: Epithelial Hyperplasia in Congenital Cystic Kidneys, J. Urol. **4**:195, 1920.

32. Von Mutach, A.: Beitrag zur Genese der congenitalen Cystennieren, Arch. f. path. Anat. u. Physiol. **42**:46, 1895.

33. Berner, O.: Die Cystenniere, Jena, 1913.

34. I am indebted to Dr. W. G. MacCallum for suggesting this use of reconstruction methods in the study of the pathology of the tubule, and for much criticism and advice in the course of this study.

flattened as a result of distention or pressure. The epithelium was granular and in some of the cysts had become completely degenerated, filling the tubule with granular debris. Intercommunication between these saccular dilatations was for the most part quite free although in some cases there was constriction by intervening bands of interstitial fibrous tissue.

This dilated portion of the tubule occupied the outer fourth or fifth of the kidney. The loops of Henle were of nearly uniform caliber throughout. The ascending limb of the loop of Henle and the distal convoluted tubule occasionally showed slight dilatation but this did not approach the cystlike character observed in the proximal convoluted tubules. The majority of the tubules showed well developed loops of Henle and opened into a collecting tubule in the usual manner. In others there was no loop of Henle and the descending portion of the tubule opened directly into the collecting tubule in the vicinity of the pelvis. The structure of these latter tubules was very suggestive of the type of embryonic tissue described by Traut.[35] Both types of tubule showed much the same degree of cystic dilatation and apparently were equally affected by the pathologic process.

The cysts in the kidney were not retention cysts for the changes in the tubules were changes in form and not of structure. There was no evidence of the type of developmental defect in the tubules that is reported as associated with congenital cystic kidney. Hydronephrosis follows obstruction in the urinary tract but this is associated with atrophy and not with dilatation of the individual tubules.

The kidneys in the present cases were remarkable because of their small size. All degrees of failure in the renal anlage have been described, from complete absence of the kidney to relative hypoplasia on the one side or the other. Cystic change is present in such rudimentary kidneys as in the case reported by Sternberg[36] and there is no sharp distinction between that condition and the hypoplastic cystic kidneys reported on by Von Mutach, Staemmler, or Schaefer.[37]

In the present case the kidneys were greatly reduced in size and the cortex was much thinner than normal. The glomeruli were greatly reduced in numbers. No attempt was made at enumeration but it is evident that there was but a fraction of the normal number of renal tubules present. The kidneys present some slight evidence of inflammatory changes but this does not explain the reduction in the number of tubules. Particularly striking is the absence of atrophic changes in the tubules, especially when this kidney is compared with one from a case of chronic diffuse nephritis. The small size of the kidneys is due to a failure in development rather than to degeneration or atrophy of these organs. Clinically this case presented evidences of a marked renal insufficiency. The tubules showed some evidences of epithelial hyperplasia though this was never extreme and there were no papillomatous changes. McKinlay has pointed out that such changes are to be interpreted as a compensatory hyperplasia consequent to the renal insufficiency. The dilatation of the convoluted tubules must likewise be considered as an active process associated with functional hypertrophy.

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[35] Traut, H. F.: Personal communication to the author. I am greatly indebted to Dr. Traut for his dissection of the tubules and confirmation of the author's findings in this case.

[36] Sternberg, C.: Zur Kasuistik der Nierendefekte und Miszbildungen des Urogenitalapparates, Wien. klin. Wchnschr. **20:**130, 1907.

[37] Schaefer, F.: Ueber eine hypoplastiche und eine partielle Zystenniere, Frankfurt. Ztschr. f. Pathol. **26:**128, 1921.

SUMMARY

A case is reported of congenital cystic kidney in a girl, aged 3 years. The clinical findings were the same as occur in chronic diffuse nephritis of congenital origin. The pathologic picture was that of bilateral hypoplasia of the kidneys with cyst formation. The renal tubules were characterized by marked cystlike dilatations, especially in the proximal convoluted tubules. There was no evidence of obstruction and the dilatation apparently was secondary to functional hypertrophy of the tubules. It should be emphasized that the clinical picture was determined by the functional insufficiency rather than by the pathologic changes in the kidney.

ULTRAVIOLET RADIATION IN RICKETS

EFFECT ON THE CALCIUM AND INORGANIC PHOSPHORUS CONCENTRATION OF THE SERUM *

B. KRAMER, H. CASPARIS AND J. HOWLAND
BALTIMORE

Huldschinsky[1] has shown conclusively that when children suffering from rickets are exposed repeatedly to the rays of the mercury vapor quartz lamp, healing of the rachitic process ensues. The changes were demonstrated by means of roentgenograms. The work has been amply confirmed by others. Howland and Kramer[2] have reported the observation that the inorganic phosphorus of the serum is markedly reduced in uncomplicated rickets and that the concentration of this substance rises to normal or slightly above normal limits following the regular administration of cod liver oil. Iversen and Lenstrup[3] have made a similar observation with regard to the acid soluble phosphorus of the plasma. In a previous paper[2] the importance of a normal inorganic phosphorus concentration for the orderly progress of calcification has been emphasized. McCollum, Park and their associates have produced rickets in rats by administering a diet containing an excess of calcium but deficient in phosphorus and the unidentified antirachitic factor present in cod liver oil. Analyses by Kramer and Howland[5] have shown that the concentration of inorganic phosphorus in the serum of such animals is reduced far below the normal level, while the calcium concentration remains normal. The concentrations of calcium and of inorganic phosphorus in the serum of these animals and in those of children suffering from rickets are essentially the same. Exposure of such animals to ultraviolet light, whether emanating from the mercury

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* From the Harriet Lane Home and the Department of Pediatrics, The Johns Hopkins University.

1. Huldschinsky, K.: Heilung von Rachitis durch künstliche Höhensonne, Deutsch. med. Wchnschr. **45**:712 (June) 1919. Die Behandlung der Rachitis durch Ultraviolett Bestrahlung, Ztschr. f. orthop. Chir. **39**:426, 1920.

2. Howland, J., and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

3. Iversen, P., and Lenstrup, E.: Förste Ved. Nordiske Kongres for Paediatri, 1919, p. 79.

4. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: Studies on Experimental Rickets. VII. The Production of Rickets by Diets Low in Phosphorus and Fat-Soluble A. J. Biol. Chem. **47**:507 (Aug.) 1921.

5. Kramer, B., and Howland, J.: The Influence of Diet on the Concentration of Phosphorus and Calcium in the Serum of Rats, Proc. Soc. Biol. Chem. **5**:21, 1921. Howland, J., and Kramer, B.: Factors Concerned in the Calcification of Bone, Proc. Am. Pediat. Soc., 1922.

vapor quartz lamp, the cadmium spark, or the ferric chromium condenser spark results in an increase of the inorganic phosphorus of the serum and the appearance of fresh deposits of calcium in the bones. The changes are identical with those which occur in rachitic children when cod liver oil is administered. In a recent communication Gutman and Franz[6] state that they have found an increase in the inorganic phosphorus of whole blood of rachitic rats after exposure to ultraviolet rays. Hess and Unger[7] report the cure of rickets in children and the

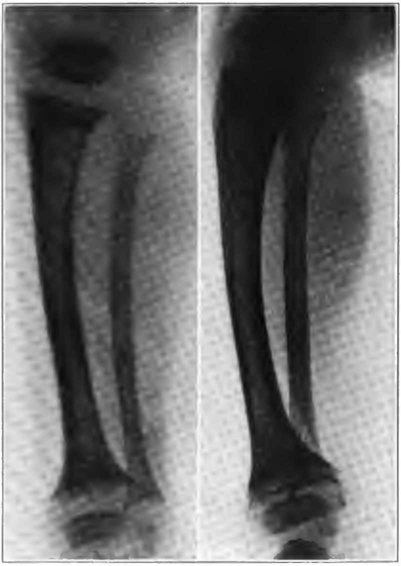

Fig. 1.—Radius and ulna of G. W. (Case 1) before (Jan. 31) treatment; thirty days after (March 7) treatment, and forty-four days after (March 21) treatment.

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[6] Gutman, M. B., and Franz, V. K.: Observations on the Inorganic Phosphate of Blood in Experimental Rickets in Rats, Proc. Soc. Exper. Biol. & M. **19**:171, 1922.

[7] Hess, A. F., and Unger, L. J.: Use of the Carbon Arc Light in the Prevention and Cure of Rickets, J. A. M. A. **78**:1596 (May 27) 1922.

prevention of rickets in rats by means of a carbon arc light. They report also a slight increase in the inorganic phosphorus of the blood of children so treated.

The observations with children that we have to report were made as a continuation of our observations on rachitic animals. Radiation was accomplished by means of a mercury vapor quartz lamp. The spectrum of the light from this lamp showed in addition to the rays of longer wave length, bands of considerable intensity in the second ultraviolet region (from 2,900 to 1,850 Aengstrom units). Of these, rays having a wave length of about 2,560 Aengstrom units gave the most intense band.

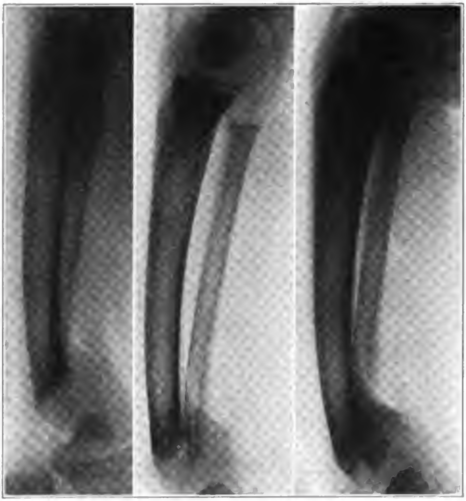

Fig. 2.—Tibia and fibula of R. H. (Case 2) before (Jan. 18) treatment; forty-two days after (March 7) treatment and fifty-six days after (March 21) treatment.

Five children, four colored and one white, were treated by these rays. They were exposed at a distance of 50 cm. every day, at first for five minutes and then the length of exposure was rapidly increased to twenty minutes. On alternate days the ventral and dorsal aspects of the body were radiated. The eyes were carefully protected. The amount of current employed was 8 ampères.

Roentgenograms were made before and several times during the course of treatment. Determinations of the calcium and inorganic phosphorus of the serum were made at least three times with each patient, once before and twice during treatment.

SUMMARY

Five children showing clinical evidences of rickets, confirmed by roentgenographic examination of the bones, were treated by systematic exposure to the rays from the mercury vapor quartz lamp. This was followed in every instance by healing of the rachitic process in the bones. The inorganic phosphorus concentration of the serum of these children was low (from 2.7 to 3.2 mg.) before the treatment was begun and gradually increased to a maximum of 6 mg. with the appearance of calcium deposition in the bones. So far as could be judged, healing of the bones following radiation occurred at about the same time as it does after the administration of cod liver oil. The changes in the phosphorus concentration of the serum were identical with those observed after cod liver oil treatment. The pigmented skin of the negro child did not interfere with the action of the light rays. The colored children required no more intensive treatment to bring about healing than did the white children.

REPORT OF CASES

Case 1.—G. W., white, aged 7 months, a premature child; evidence of rickets not marked.

Jan. 31, 1922: Roentgenogram showed slight irregularity of extremities of radius and ulna.

February 2: Calcium, 8.5 mg. per 100 c.c. of serum; inorganic phosphorus, 3 mg.

February 5: Treatment begun.

March 7: Roentgenogram showed marked irregularity of lower extremities of radius and ulna, evidently brought about by considerable deposition of lime salts. This had produced distinct cupping.

March 8: Calcium, 10.1 mg. per 100 c.c. of serum; inorganic phosphorus, 5.8 mg.

March 21: Roentgenogram showed evidences of healing still more marked.

March 21: Calcium, 10.3 mg. per 100 c.c. of serum; inorganic phosphorus, 6 mg.

Case 2.—R. H., colored, aged 10 months; marked clinical evidences of rickets.

Jan. 18, 1922: Roentgenogram showed very severe rickets. Centers of ossification poorly marked. Extremities of bones very indistinct.

January 21: Calcium, 9.4 mg.; inorganic phosphorus, 2.7 mg.

January 24: Treatment begun.

March 7: Roentgenogram showed evidences of deposition of lime salts producing double lines at extremities of bones. Centers of ossification becoming plain.

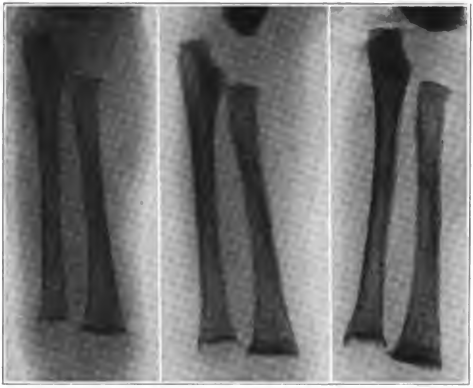

Fig. 3.—Tibia and fibula of E. F. (Case 3) before (Feb. 2) and forty-three days after (March 21) treatment.

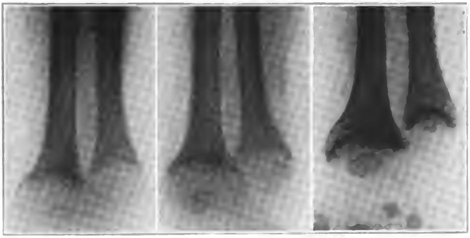

Fig. 4.—Radius and ulna of F. P. (Case 4) before (Jan. 16) treatment; twenty-seven days after (Feb. 20) treatment, and forty-two days after (March 7) treatment.

March 8: Calcium, 9.3 mg.; inorganic phosphorus, 3.4 mg.

March 21: Roentgenographic evidences of healing plain.

March 21: Calcium, 10.1 mg.; inorganic phosphorus, 6.2 mg.

Case 3.—E. F., colored, aged 26 months; marked clinical evidences of rickets.

Feb. 2, 1922: Roentgenogram showed striking evidences of rickets of long standing.

February 6: Calcium, 10.6 mg. per 100 c.c. of serum; inorganic phosphorus, 3 mg.

February 6: Treatment begun.

March 21: Roentgenogram showed marked evidences of healing. Deposition of lime salts at extremities of bones now plain.

March 22: Calcium, 9.5 mg.; inorganic phosphorus, 6 mg.

Case 4.—V. P., colored, aged 18 months; marked clinical evidences of rickets.

Jan. 16, 1922: Roentgenogram showed cupping of lower ends of both radius and ulna. Centers of ossification at wrist indistinct.

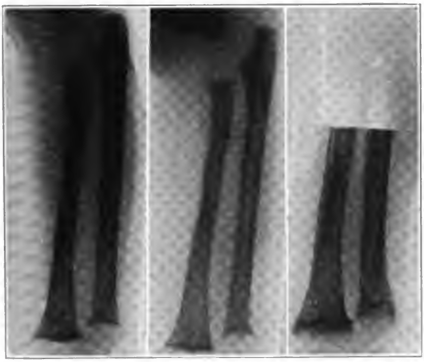

Fig. 5.—Radius and ulna of M. C. (Case 5) before (Dec. 20) treatment; after forty days (Jan. 30) insufficient treatment, and after forty-nine days (March 21) intensive treatment.

January 18: Calcium, 9.2 mg. per 100 c.c. of serum; inorganic phosphorus, 3 mg.

January 24: Treatment begun.

February 20: Roentgenogram showed early but definite evidences of healing.

February 23: Calcium, 10.1 mg.; inorganic phosphorus, 4.6 mg.

March 7: Roentgenogram showed marked evidences of healing.

March 8: Calcium, 10.2 mg.; inorganic phosphorus, 6.6 mg.

Case 5.—M. C., colored, aged 5 months. Clinical diagnosis on admission was rickets and tetany.

Dec. 20, 1921: Roentgenogram showed mild but definite rickets. Cupping at lower end of the ulna, irregularity of the lower end of the radius.

December 21: Calcium chlorid was administered, 1 gm. every four hours, for several days. It was then reduced to 0.5 gm. Radiations with ultraviolet rays were also employed. The time of exposure was short (from 5 to 10 minutes); the intensity was slight (amount of current, 4 amperes) and the child was exposed only three times a week.

Jan. 21, 1922: Calcium, 8 mg. per 100 c.c. of serum; inorganic phosphorus, 3.2 mg.

January 30: Roentgenogram showed no change.

February 1: As it was obvious that no improvement had taken place more intensive treatment was employed as outlined in the first part of the paper.

February 27: Roentgenogram showed definite evidence of healing.

March 6: Inorganic phosphorus, 6.2 mg.

March 21: Roentgenogram showed almost complete healing.

March 21: Calcium, 9.8 mg.; inorganic phosphorus, 6.1 mg.

THYMUS APOPLEXY

AN UNUSUAL MANIFESTATION OF HEMORRHAGIC DISEASE OF THE NEWLY BORN *

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The thymus gland is richly supplied with blood vessels [1] which are readily engorged and often contribute considerably to the enlargement of the gland.[2] This congestion is especially apt to occur whenever there is a general circulatory stasis.[3] There is little supporting tissue for the rich network of capillaries in and about the individual lobules so that hemorrhages occur readily.[3] These may be scattered, small and petechial in character, or they may appear as large effusions of blood localized or diffused throughout the substance of the organ. The former are common, especially in asphyxial conditions, in acute infections and in hemorrhagic diseases. The latter are relatively rare and were first noted by Friedleben [4] in his basic monograph in which he applied the term "Apoplexien" to these more extensive hemorrhages. Such an "apoplexy" may follow the hyperemia associated with simple hyperplasia of the gland and may give the appearance of a hemorrhagic infarct.[5] Inasmuch as but few cases are in the literature a review of these is given.

Friedleben [4] noted the occurrence of these extensive hemorrhages in the thymus gland in cases of protracted and difficult labor and regarded them as traumatic in origin. He also gave a detailed description of a 5 month old infant which died suddenly during convalescence from an attack of diarrhea. The infant had taken its bottle during the night and was found dead in the morning. The necropsy showed subserous hemorrhages in the pleura and pericardium. The thymus gland was diffusely infiltrated with blood. No microscopic examination was made.

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1. Pigache, R., et Worms, G.: Circulation du lobule thymique, Bull. et mém. soc. Anat. de Par. **12**:837, 1910.

2. Hart, C.: Thymus Studien: Pathologie der Thymus, Arch. f. path. Anat. **214**:1, 1913.

3. Wiesel, J.: Pathologie des Thymus, Ergebn. der allg. Path. u. path. Anat. **15**: Pt. 2, 416, 1912.

4. Friedleben, A.: Die Physiologie der Thymusdrüse in Gesundheit und Krankheit, Frankfurt A. M. Literarische Anstalt. 1858.

5. Marfan, A. B.: Pathologie du Thymus, Arch. de méd. d. enf. **13**:801, 1910.

Several cases are cited by some authors with such meagre data that their value is doubtful. Raudnitz[6] cites the case of a child, 5 months old, dying with asphyxial symptoms. At the necropsy there was a large thymus, infiltrated with blood. He also cites Kopp's case of an infant 33 days old, with hemorrhages from the umbilicus, dying nine days later. The postmortem examination showed a pneumonia, a bloody effusion about the umbilicus and a bloody tumor mass covering the upper anterior surface of the heart and containing thymus elements. Both Friedleben[4] and Wiesel[3] note Weber's case of a several months' old infant dying after several severe abdominal cramps. The necropsy showed a fresh hemorrhage in the thymus gland. Wiesel also cites Bonnet's case occurring in a man who died suddenly and in whom the thymus gland was found enlarged and infiltrated with blood. The same author mentions Beneke's case occurring in the stillbirth in which the fetus was forcibly extracted. There was a hemorrhage in the thymus and also over the surface of the brain. Bauer's case is also cited. The patient was a young soldier who died suddenly without any apparent cause. The thymus gland was found infiltrated with blood.

Barensprung[7] described the case of an infant which was struck by its syphilitic mother the day after its birth, and had hemorrhages from the navel and ecchymoses in the shoulders, arms and hands. Death occurred eight days after birth. The necropsy showed numerous subcutaneous hemorrhages, especially in the cheek, and on the hands and chest. The umbilical vein was occluded by a thrombus. The thymus was very large and infiltrated with blood, and also contained a cavity filled with a soft red blood clot. There was also a bloody fluid in the pericardium and focal hemorrhages in the kidney medulla. The latter also contained uric acid infarcts.

Raudnitz[6] reported two cases. One patient was an infant with a syphilitic mother. Following birth a hematoma developed over the right parietal bone. The infant was jaundiced but otherwise was apparently well to the forty-fifth day when it suddenly became pale, respirations were rapid, pulse 120 and hemorrhages appeared in the hard palate. The child refused food. Vomiting occurred and was followed by collapse and death. Blood clots were found in the occipital and temporal fossae. The left pleural cavity contained much clotted blood. The mesenteric glands were enlarged and contained hemorrhages. The left lobe of the thymus was enlarged, measuring 5 cm. in length, and contained extensive hemorrhages. The right lobe was normal.

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6. Raudnitz, R. W.: Hemorrhagien der Thymus, Arch. f. Kinderh. **4**:21, 1883.
7. v. Barensprung, F.: Die Hereditare Syphilis, Berlin, 1864.

The second case was that of an infant showing blood in the stools and punctate hemorrhages in the palate when ten days old. Dyspnea then developed, followed by death five days later. The necropsy showed a blood clot over the left cortex and the pia was infiltrated with blood. Hemorrhages were present in both lower lobes of the lungs, in the pericardium and in the tissue about the thymus and adjacent esophagus. The left lobe of the thymus was enlarged and contained a hematoma the size of a walnut.

Durante[8] also described two cases. In the first case the infant was born dead following a protracted labor. The thymus gland was enlarged, weighing 21 gm. The gland showed intense congestion and also hemorrhages, especially within the lobules, in some of which the entire medullary substance was so extensively replaced by blood that only a narrow rim of cortical substance remained. The blood was not collected in a single continuous mass but diffusely infiltrated the gland, separating the architectural elements.

The second case was in a premature child which died suddenly on the fourth day without any apparent cause. The thymus gland was enlarged, weighing 20 gm. There were numerous hemorrhages some of which destroyed several lobules. Some of the foci infiltrated with blood showed organization indicating that some of the effusions of blood were older than others.

Schlesinger[9] described a hemorrhage in the thymus gland, occurring in a syphilitic infant who had a persistent umbilical hemorrhage from which it died on the ninth day. The necropsy showed fibrous induration of the lungs, liver and pancreas, indicating congenital syphilis. The thymus gland was enlarged and on the left side contained a small cavity filled with clotted blood. In addition there were several smaller hemorrhages in the tissue surrounding the larger one. These hemorrhages involved the parenchyma and the stroma but the medullary substance showed more disintegration than the cortex. Hassall's corpuscles were numerous and persisted even in the masses of blood when all other thymus elements had disappeared. Focal necroses were also present.

Mendelsohn[10] contributed the most complete discussion of this subject and gave a detailed description of a thymus hemorrhage occurring in a syphilitic infant dying five hours after birth. There was a pemphigous eczema on the soles of the feet and the palms of the hand.

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[8] Durante, G.: Hemorrhages et scleroses due thymus chez les enfants nouveau-nes, Compt. rend. Soc. de biol. **48**:282, 1896.

[9] Schlesinger, E.: Die Erkrankungen der Thymusdrüse bei der hereditaren Syphilis, Arch. f. Kinderh. **26**:205, 1899.

[10] Mendelsohn, L.: Ueber die Apoplexie der Thymusdrüse, Arch. f. Kinderh. **44**:1, 1906.

The lungs were indurated and the liver enlarged. The thymus gland weighed 8.7 gm. The left lobe was normal. The right lobe contained a cavity about the size of a hazelnut filled with partly clotted blood. There were also a few smaller hemorrhages. Microscopic examination showed typical syphilitic changes in the lungs and the liver. The vessel walls were thickened, especially the adventitia. The wall of the blood containing cavity was composed of three layers, the inner one only being composed of thymus elements. This cavity was a preformed cyst into which a hemorrhage had occurred.

Winkler[11] reported a case occurring in a male infant which was well at birth, but developed dyspnea, cyanosis and cardiac weakness, and finally death ensued on the fourth day. There was a subpial hemorrhage on the right side. The thymus gland was enlarged and on section showed many hemorrhages uniformly distributed throughout the gland.

Klose[12] described a diffuse hemorrhagic infiltration of the thymus gland in a boy, 9 years old, who had whooping cough and died from asphyxia following a severe paroxysm of coughing. The gland was much enlarged. No other hemorrhages were noted. A tracheotomy was performed but was of no avail.

Hart[2] noted a case of diphtheritic laryngitis in which the thymus gland was entirely hemorrhagic and infarcted.

Pappenheimer's case[13] occurred in a 7 week old syphilitic infant who had a general purpuric eruption, an interstitial pneumonia and a well marked status lymphaticus. The thymus gland was enlarged, weighing 25 gm., and was diffusely infiltrated with blood. There were also extensive areas of necroses. The cytoplasm of the reticular cells contained yellow pigment granules. The small thymus elements were not abundant. There were no Hassall's corpuscles. The parenchyma was composed mostly of large reticular epithelial cells with indifferent cell outlines and extensive intercellular connections. The usual lobulation of the thymus gland was absent. There was evidently a delay in the development of the gland.

The last case reported was that of Frazier[14] in which the thymus of a syphilitic male stillbirth was enlarged and contained scattered hemorrhages. The upper half of the gland contained a spherical cavity, the size of a dime, distended with fluid blood. In the lower half there was a cavity the size of a quarter containing grayish white purulent matter. There was no cyst formation. There were multiple granulomas in the cortex.

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[11] Winkler: Zur Pathologie der Thymusdrüse, Verhandl. d. deutsch. path. Gesellsch. **13**:266, 1909.

[12] Klose, H.: Chirurgie der Thymusdrüse, 1912, in Frankfurt a. M.

[13] Pappenheimer, A.: A Contribution to the Normal and Pathological Histology of the Thymus Gland, J. M. Research **22**:1, 1910.

[14] Frazier, J. F.: The Visceral Changes in Congenital Syphilis, J. A. M. A. **77**:1623 (Nov. 19) 1921.

An analysis of the nineteen cases found in the literature is interesting. It is probable that more cases have been reported but are buried under general and obscure titles. In fact, only five cases of this series were reported under a specific title while the remainder were gleaned from papers on either the pathology of the thymus gland or congenital syphilis. A small proportion only (seven cases) had a complete description. In some of these a thorough microscopic study was not made. In all cases but two there was a note on the nature of the hemorrhage. In eleven cases it was diffused throughout the gland; in the remainder it was localized to one or more foci. The age was noted in all but one of the cases and varied from stillbirths to young adults. Three cases occurred in stillbirths, three in infants less than one week old; six infants were between this age and 3 months; three cases occurred between 3 and 6 months, one child was 9 years of age and two patients were young male adults. It is worth emphasizing that with the exception of three cases, two of which occurred in young men, all the other cases occurred in infants under 6 months.

The nature of the death was noted in thirteen cases. In seven cases it was sudden, but no other information was available. In two instances it followed persistent hemorrhages. In two cases there was dyspnea; in two, asphyxia, and in one case severe cramps. The presence or absence of other hemorrhages was not noted in eight cases; in three cases they were absent; in two cases there were hemorrhages in the umbilicus; in five cases, subserous hemorrhages, and in five cases cerebral hemorrhages were associated.

Regarding the presence of visceral lesions no information was available in ten of the cases. In two cases they were reported as being absent. In three cases an interstitial pneumonia was noted. One infant had pneumonia, one had diphtheretic laryngitis and another had lung infarcts. Regarding the possibility of syphilis being present no information was available in seven cases. In six cases a definite diagnosis of hereditary syphilis was made. In two instances there was a history suspicious of syphilis. In five cases it was absent. In five cases there was a history of trauma; in four cases it could be excluded, while in the others no note regarding trauma was made.

REPORT OF CASES

Case 1.—Baby R., colored, male, aged 4 days, one of twins, was admitted to Bell Memorial Hospital. Sept. 19, 1920.

Family History.—Father, aged 43, living and well. Wassermann negative. Mother, aged 37, living and well. Three sisters, ages 8, 6 and 4 years, respectively, living. The eldest shows glandular enlargement and with questionable

Hutchinsonian teeth, but with a negative Wassermann. The youngest sister is markedly undernourished. There were two brothers. One aged 2 years had marked rickets and a negative Wassermann. The other was the twin brother of the patient and was apparently normal.

Past History.—During pregnancy the mother was unusually short of breath and had much distress. She felt that the baby was transverse in position. The pregnancy went to full term. The patient was the second born of twins and was delivered from a breech presentation with considerable traction and difficulty. On the second day the mother noticed bleeding from the mouth and persistent dark pasty stools. There were no convulsions. The infant fretted a great deal. The baby refused all food and was brought to the hospital on the fourth day with convulsions.

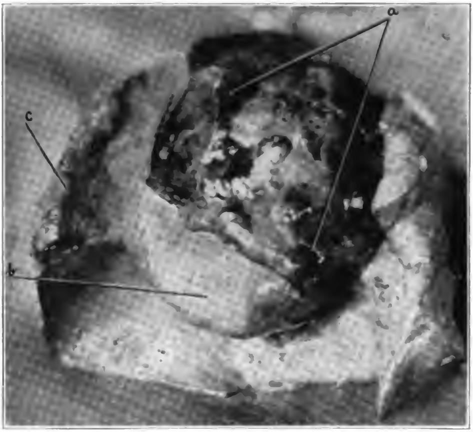

Fig. 1.—Photograph of the thymus gland of Case 2, showing its relation to the heart and to the lungs. (a) Thymus gland enlarged and infiltrated with blood; (b) apex of heart; (c) anterior edge of upper lobe of the right lung.

Physical Examination.—The baby was small and critically ill with a temperature of 102.5 F., and with the head drawn back. The arms and legs were very rigid and the fingers markedly flexed in a position of tetany. The skin and sclera showed a definite icterus. Clusters of miliary vesicles were present over the chest, neck and upper arms. Both fontanels were open but not depressed. There was no craniotabes or overriding of the cranial bones at the sutures. There was a lateral nystagmus of both eyes. Ears and nose were normal. The mouth could not be opened wide enough to inspect the throat, but the tongue was covered with a white milky coat. The heart was very rapid but no murmurs could be heard. The lungs showed no definite impairment. The breath sounds were very rapid and of a Cheyne-Stokes character. The abdomen was full and held very tense. The liver and spleen could not be felt. The genitalia were normal, except for phimosis. The lymph nodes were not prominent.

A puncture of the lateral ventricle was made through the anterior fontanel and 20 c.c. of unchanged blood was obtained. This blood clotted very slowly and the clot was soft in consistency. The red cells settled out. A Wassermann was done on this blood but was negative. The patient was moribund on entrance and died ten hours later.

Clinical Diagnosis.—Cerebral hemorrhage from a birth injury associated with hemorrhagic disease of the new-born.

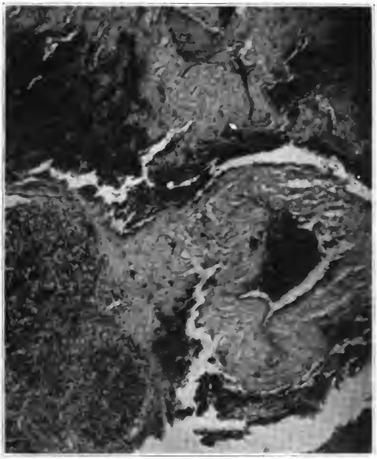

Fig. 2.—Photomicrograph of a thrombus in a large vein of the thymus gland in Case 1. Note also the hemorrhage in the surrounding tissue and the endothelial hyperplasia in the small lymph node which is embedded in the capsule of the thymus gland.

NECROPSY REPORT

Macroscopic Examination.—The body is that of a well developed male infant showing generalized icterus, a fine vesicular eruption over the neck and chest and petechial hemorrhages on the buttocks. Bloody fluid is present in both pleural cavities, 30 c.c. on the right side, less on the left. There is a large red hemorrhagic mass with a smooth outer surface in the upper mediastinum extending from the lower border of the thyroid to the lower third of the pericardium and from the hilum of one lung to that of the other. It is composed mostly of an enlarged thymus diffusely infiltrated with blood, weighing 27.4 gm. and measuring 6x4x1.8 cm. The lobes of the thymus are indistinct. The mass is firm in consistency. The cut surface has a dark red color with a network of grayish white markings which give it a lobulated appearance. In some areas the hemorrhage involves the parenchyma of the organ; in others it is limited to the stroma leaving islands of thymus tissue embedded in a mass of blood. The hemorrhagic infiltration extends into the soft tissues about the trachea, esophagus and hilum of the lung.

Hemorrhages were also present in other viscera. Scattered subpleural hemorrhages in the lungs extended a short distance into the substance of the lungs. Small hemorrhages were present in both the pericardium and in the myocardium. The kidneys showed numerous wedge shaped hemorrhages involving both cortex and medulla. Extravasations of blood were also present in the diaphragm along the attachment of the pericardium and in the medulla of both suprarenal glands. The cerebrospinal fluid over the surface of the brain was blood tinged. Both lateral ventricles were distended and dilated with bloody fluid. This was particularly true of the right lateral ventricle which contained 50 c.c. fluid blood in addition to a soft blood clot continuous with one in the left lateral ventricle which was nearly occluded by the blood clot. Fluid blood was also present in the other ventricles. The right parietal lobe was considerably softened due, in part, to the dilatation of the right lateral ventricle and, in part, to the extravasation of blood into the brain substance external to the posterior part of the right lateral ventricle.

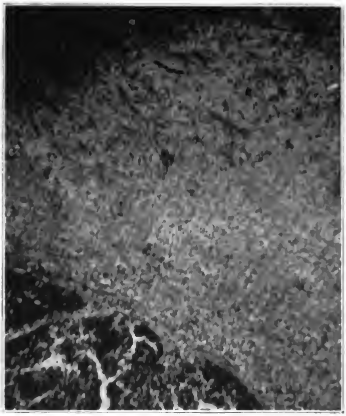

Fig. 3.—Photomicrograph of necrosis, hemorrhage and organization in the stroma of the thymus gland in Case 2. On each side of this thick band of connective tissue there are lobules of the thymus parenchyma infiltrated with red blood corpuscles.

Some portions of the lungs did not contain air. The consistency was tougher than usual. There was an unusually distinct lobulation. The foramen ovale of the heart was widely open. The liver showed some hemorrhages just beneath the capsule. Numerous brick red crystals (uric acid) were present in the pyramids of the kidneys.

Microscopic Examination.—Heart: Vacuoles are present in many of the muscle fibers. There are also small hemorrhages in the myocardium.

Lungs: Bands of cellular fibrous tissue subdivide the lung tissue into distinct lobules. The lung framework is markedly thickened and infiltrated with leukocytes, most of which are mononuclear in type. Small hemorrhages occur in the interstitial tissue especially about the hilum. The capillaries are engorged. The alveolar epithelial cells are swollen, small vacuoles are numerous in the cytoplasm of many cells and many others are desquamated into the alveolus. Red blood cells are present in some of the alveoli. Many air sacs contain desquamated epithelial cells and serum but relatively few leukocytes. The adventitia of the blood vessels is thickened and the lumen is often reduced in size.

Liver: The fibrous tissue is increased in the portal spaces. The liver cells are swollen and contain many small vacuoles. Various types of leukocytes are scattered throughout the lobule. A few eosinophil cells are also present. There are a few foci of myeloid cells in the sinusoids.

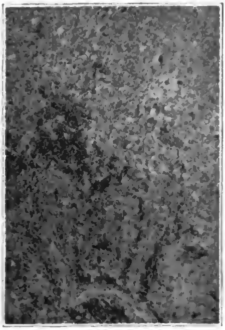

Fig. 4.—Photomicrograph of the perivascular inflammatory reaction and endothelioid hyperplasia in the stroma of the thymus gland in the second case.

Pancreas: The parenchyma is incompletely developed. Many of the acinar cells are degenerated. The islands of Langerhans are small and indistinct. The stroma is much more abundant than is usual.

Spleen: There is diffuse fibrosis throughout the pulp. The sinusoids are unusually prominent. There is marked endothelial hyperplasia. The walls of the vessels are thickened. The malphigian bodies are small and obscure.

Kidneys: They are infantile in type. The epithelial cells of some convoluted tubules are swollen and others are disintegrated. There is some proliferation and desquamation of the cells of the collecting tubules. The glomeruli are numerous. There are no red blood cells in the capillaries of the glomeruli. The endothelial cells of the latter are swollen. The interstitial tissue is abundant and shows many fibroblasts. There is diffuse congestion and infiltration with leukocytes some of which occur in foci and include polymorphonuclear cells as well as lymphoid cells. Some eosinophil cells also occur. The walls of the vessels are thickened. Extravasations of blood are limited to the interstitial tissues. No red blood cells are present in the tubules.

Suprarenals: The medulla shows marked congestion and considerable diffuse hemorrhage. It also shows beginning postmortem autolysis. In the cortex the stroma is unusually abundant.

Thyroid: Most of the follicles are underdeveloped and contain none or very little colloid. The stroma is very cellular and abundant. It contains numerous leukocytes both of the mononuclear and the polymorphonuclear types.

Lymph Nodes: These show marked congestion; otherwise unnoteworthy.

Cerebral cortex: There is a diffuse extravasation of blood throughout the white matter.

Thymus: There is a marked increase in the stroma separating the parenchyma into unusually distinct lobules. This increase is, in part, due to proliferation of the connective tissue as indicated by numerous fibroblasts and, in part, to the infiltration with blood. In some portions this hemorrhagic infiltration is so extensive that the lobules of thymus tissue appear as islands in a mass of blood cells. In some areas the stroma is infiltrated with a purulent exudate, in others it shows focal areas of necrosis. The larger vessels show a very thick wall due mostly to thickening of the adventitia. In several of them the lumen is almost completely occluded by cellular thrombi. In the perilobular tissue there are also foci of lymphoid and polymorphonuclear cells with begining necrosis suggesting miliary gumma.

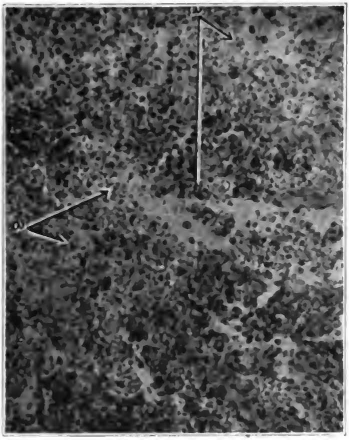

Fig. 5.—Photomicrograph of lymph node embedded in the capsule of the thymus gland in Case 2, showing dilated lymph sinuses containing many large endothelial phagocytes (a) which have engulfed many red blood corpuscles.

The parenchyma shows marked congestion and diffuse hyperplasia of the reticular epithelial cells. In fact, so marked is this hyperplasia of these large pale cells that in many foci few lymphoid cells remain. There is also proliferation and swelling of the endothelial cells of the vessels. Hassall's bodies are numerous and show a tendency to cystic degeneration and dilatation. Often these cystic structures contain a purulent exudate. Some of the lobules are almost entirely destroyed by hemorrhage, only a narrow rim of the cortical substance persisting. The hemorrhages apparently occur first in the medullary substance which seems more readily broken down than the cortex. Throughout the lobules there is diffuse infiltration with leukocytes, including polymorphonuclear and eosinophil cells as well as lymphoid cells. Karyorrhexis of many of the nuclei occurs, in fact there are all stages between this diffuse leukocytic infiltration, necrosis and hemorrhage. In other words, the hemorrhage is preceded by necrosis. Often the lobule has been almost replaced by blood, except a narrow rim of cortical tissue and a few Hassall's bodies embedded in the mass of red blood cells. Some of the smaller veins are distended with leukocytic thrombi.

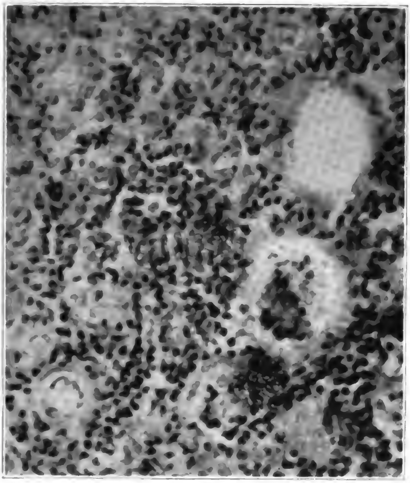

Fig. 6.—Photomicrograph of two dilated Hassall bodies in the thymus gland in Case 1. This area shows no hemorrhage but shows many scattered polymorphonuclear leukocytes and considerable proliferation of the epithelioid cells. Note the normal Hassall body in the lower left corner.

Bacteriologic Examination.—Unfortunately no cultures were made at time of the necropsy. Bacterial stains of sections of the thymus showed occasional coccoid bodies but no definite organisms. No spirochetes were found.

Anatomic Diagnosis.—Cerebral hemorrhage; diffuse hemorrhagic infiltration of the thymus gland; multiple hemorrhages in the lungs, suprarenals, kidneys and heart; subserous hemorrhages into the pleura, pericardium and capsule of liver; chronic interstitial pneumonia; parenchymatous degeneration of heart, liver, kidneys and pancreas; thrombosis of vessels of thymus, acute inflammation and focal necroses of the thymus gland.

CASE 2.—Baby P., white, male, aged 6 weeks, was admitted to the contagious hospital Jan. 1, 1921, with a provisional diagnosis of meningitis.

Family History.—The father was apparently in good health. Mother, aged 19 years, primipara, had a four plus Wassermann. Physicial examination of her heart gave findings suggestive of an aortitis.

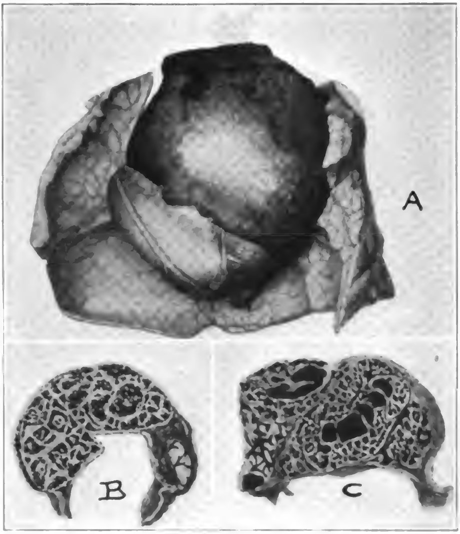

Fig. 7.—A. Drawing of the thymus in Case 2, showing its exact size and its relation to the heart and lungs.

B. Drawing of a cross section through the thymus gland of Case 1.

C. Drawing of a cross section through the thymus glands of Case 2.

Past History.—The baby was delivered by a dry labor which, however, was not unusually protracted, and was charted as a normal baby although the birth weight was only 5 pounds 8 ounces. The usual initial loss of weight brought the weight down to 4 pounds 9 ounces, and on the sixth day it was up to 5 pounds, remaining stationary the remainder of the stay in the hospital (ten days). From the third to the sixth day the temperature ranged from 103 to 106 F. Before and after this period it was normal. The temperature fell to normal when diluted cow's milk was given with the breast feeding. At three weeks of age the patient was again examined and found to be a normal breast fed baby, except that it was fretful and colicky.

Present Illness.—One week before entering the hospital (5 weeks of age) the baby had a yellow color, had not gained weight and was in poor condition. It cried much, took the breast poorly and was very restless. Two days before admission there was some bleeding from the nose and mouth and the stools had become black. The night before entering the hospital the baby's condition became worse, showing a generalized spasticity and retraction of the head, and the eyes appeared to be set and glassy.

Physical Examination.—A fretful, desperately ill, undernourished baby, lying with its head drawn back, and at times giving a characteristic meningeal cry. There was marked jaundice. The extremities were spastic and the muscles of the neck tense. The anterior fontanel bulged markedly. The right eye showed a divergent strabismus. The left eye showed a ptosis of the lid. Both pupils were unequal and dilated. There was a slight horizontal nystagmus of both eyes. The heart was normal with no murmurs but with a very rapid rate. There was a slight umbilical hernia. The thumbs of both hands were flexed on the palms and the fingers were flexed over the thumbs.

Blood Wassermann was negative. It was noted that this blood did not clot, the red blood cells settling out at the bottom. A soft clot developed later. A lumbar puncture was made but the examination was unsatisfactory. The baby continued in a state of spasticity, with an occasional convulsion, and gradually became more feeble, dying twelve hours after admission.

Clinical Diagnosis.—Cerebral hemorrhage complicating hemorrhagic disease of the new-born.

NECROPSY REPORT

Macroscopic Examination.—Unfortunately, complete necropsy data on this case are not available. Through the kindness of Dr. W. S. Campbell we received the brain, kidneys, spleen and all of the thoracic organs for study. The heart was normal. The kidneys showed marked fetal lobulation, otherwise appeared to be normal. The spleen was normal, except for marked congestion. The lungs showed a distinct lobulation with areas of dark gray partly consolidated tissue. These areas on section had an edematous transluscent appearance. Most of the lung tissue was air containing. There was a denser framework than is normal. There was also considerable hemorrhage in the hilum of the lungs, extending, on the one hand, into the lung tissue along the bronchi and, on the other hand, continuous with a large hemorrhagic mass situated in the upper anterior mediastinum. This mass is composed of an enlarged thymus markedly infiltrated with blood, extending from the hilum of one lung to that of the other and covering the greater part of the pericardium. Its outer surface is smooth and reddened but there is no free blood. This enlarged thymus weighs 28.4 gm. and measures 5 x 4.2 x 2.4 cm. It is very firm in consistency. It cuts with resistance and the cut surface has a dark red color with an interlacing network of grayish white markings giving the hemorrhagic tissue a lobulated appearance. In other areas there are islands of pale yellow tissue embedded in a hemorrhagic matrix. While the blood is diffused throughout the gland, near the center there were several clots of blood from 6 to 8 mm. in diameter. The right lobe of the thymus shows more extensive infiltration with blood than the left, and is accordingly very much larger. The capsule of the gland is infiltrated with blood. No hemorrhages were found in the other viscera. There was a thin layer of blood beneath the pia on the lateral surfaces and base of the brain but no hemorrhage in the cerebral cortex. The ventricles contained no blood.

Microscopic Examination.—Heart: Many of the muscle fibers contain vacuoles often associated with obliteration of the cross striations and even distintegration of the cytoplasm. The connective tissue is increased and contains many leukocytes, most of which appear as small dark staining round cells occasionally arranged in small foci. In the latter a few polymorphonuclear leukocytes may be seen.

Lungs: The pleura is thick. The alveolar walls are thickened, cellular and contain many leukocytes, polymorphonuclear as well as mononuclear, the latter being most abundant. The walls of the vessels, especially the adventitia, are thickened, and in some the lumen is reduced in size. Some of the bronchi are filled with a purulent exudate; others appear to be normal. The peribronchial connective tissue is unusually abundant, and in some areas it is infiltrated with blood. There is also considerable infiltration with lymphoid cells. In addition, near the hilum, there is considerable embryonic fat and clusters of large round cells resembling endothelial phagocytes containing brown pigment granules. The alveoli vary in appearance. Some are empty, others are filled with desquamated, round, alveolar epithelial cells and serum. Others contain a purulent exudate. Many show a swollen culoidal epithelial lining. In some of the bronchi there is a fibrinous exudate containing scattered red blood cells.

Spleen: There is marked congestion; otherwise the organ is normal.

Kidney: The glomeruli are numerous and the cells are swollen. Few red blood cells are seen in the capillary tufts. The tubular epithelial cells are swollen and some are disintegrated. A few of the cells are calcified. There is some fibrosis and lymphoid infiltration throughout the organ.

Aorta: There is swelling and edema of the elastic fibers of the media and infiltration of lymphoid cells especially about the vasavasorum.

Lymph nodes: The bronchial nodes are intensely congested, the sinusoids are distended and contain many large endothelial phagocytes, many of which are filled with red blood cells. There is marked swelling and proliferation of endothelial cells. Some of the larger nodes about the trachea show much the same picture. In one node the endothelial proliferation is so extensive about the periphery as to resemble a collar of tumor tissue. Besides the congestion there is also some slight diffuse hemorrhage, especially in foci containing pus cells and in which beginning necrosis is evident. The marked endothelial proliferation is associated with atrophy of the lymphoid elements.

Thymus: The architecture of the gland is exaggerated by the marked thickening of the perilobular fibrous tissue. The increase of these septa is due to extensive diffuse hemorrhage and suppuration. Foci of necrosis are present but poorly outlined. The capsule is also markedly thickened for the same reason and shows many fibroblasts and new formed capillaries, especially extending where the blood is most abundant. Some of the broad interlobular septa contain no hemorrhage but show extensive purulent exudation and occassionally poorly outlined areas of necrosis. Leukocytes of various types including polymorphonuclears and eosinophils abound in the stroma. Several small hyperplastic lymph nodes are adherent to the capsule of the thymus. In the stroma there is also swelling of the endothelial cells of the vessels and marked accumulation of lyphoid cells about these vessels. This perivascular reaction is very striking in some areas. The thymus lobules appear as islands of cellular tissue in the hemorhagic tissue. Hassall's corpuscles are numerous. There is marked congestion and hyperplasia of the reticular epithelial cells. The latter are so numerous that in some lobules few of the smaller thymic elements are left. There are numerous eosinophil cells. In many lobules there are scattered foci of lymphoid and polymorphonuclear cells showing beginning necrosis. Occasionally, small hemorrhages may be seen in these foci. In fact, there are all stages between the acute inflammatory reaction, necrosis of the center of the lobule and its almost complete replacement by hemorrhage. In some lobules the hemorrhage has destroyed the greater part so that only a narrow rim of the cortex still persists. Even in these areas the Hassall's bodies may still persist. Many of the small veins are filled with pus cells.

Bacteriologic Examination.—Negative, as in Case 1.

Anatomic Diagnosis.—Bronchopneumonia, chronic interstitial pneumonia; thymus apoplexy; subpial hemorrhage of brain; acute inflammation and focal necroses of the thymus; thrombophlebitis of veins of thymus, parenchymatous degeneration of the heart and kidneys.

DISCUSSION

The two cases are similar in many respects. Symptoms of meningeal irritation, lateral nystagmus and generalized icterus were present in both infants. Labor, while not normal, was not unduly difficult or prolonged in either case. In both cases there was a marked increase in the coagulation time of the blood. In each case the necropsy showed a cerebral hemorrhage, inflammatory changes in the lungs suggestive of syphilis and a diffuse hemorrhagic infiltration of the thymus in which the extravasation of blood was both intralobular and interlobular and was associated with suppuration, necrosis and marked proliferation of the reticular epithelial cells. The cases differ in that the second patient was much older than the first. The hemorrhages were more generalized and extensive in Case 1. Labor was more difficult in Case 1. The immediate cause of death in Case 1 was cerebral hemorrhage, while in Case 2 the bronchopneumonia was probably the more immediate factor causing death. There was considerable organization of the hemorrhage in Case 2, indicating an older process than in Case 1 in which no new capillaries or fibroblast were found. In both cases the Hassall's corpuscles were numerous but in Case 1 they were dilated and often contained a purulent exudate forming early DuBois abscesses.[15] On the other hand, Case 2 showed a striking perivascular inflammatory reaction with swelling of the vascular endothelium and also marked thrombophlebitis of the smaller veins. One of the large veins in Case 1 was partly occluded by a thrombus (Fig. 2).

The relation of these cases to syphilis is of considerable interest. Case 1 presented no positive clinical findings. The Wassermann test on the bloods of both the father and infant were negative. No examination of the mother's blood could be obtained. Several members of the family showed evidences of constitutional weakness and syphilis could not be excluded even with negative blood findings. The clinical findings in Case 2 were more suggestive of syphilis. The Wassermann reaction on the blood of the mother was strongly positive but in the case of the child it was negative. There was no opportunity to repeat this test and a single negative reaction is not conclusive. The anatomic changes in both cases, while not pathognomonic, afford strong presumptive evidence of syphilis. Examination of the tissues for spirochetes in both cases was negative but this was most likely due to improper fixation. The interstitial inflammatory changes in both lungs suggest syphilis. The lobules of the thymus gland that are not disintegrated by hemorrhage show changes in both cases that are regarded as characteristic of congenital syphilis. In both cases there was marked proliferation of the reticular epithelial cells associated with more or less atrophy of the thymic lymphocytes, a change that Simmonds,[16] Hart,[2] Hecker,[17] Schlesinger, Dudgeon[18] and Klose[12] note as a characteristic change in the thymus of congenital syphilis. Furthermore, the early stages in the formation of DuBois abscess as described by Oliver[15] were present in Case 1. While Case 2 does not show this dilatation of the Hassall bodies with the beginning formation of DuBois abscesses (which are said to be present only in fetal syphilis), it does show a very marked perivascular lymphoid infiltration and hyperplasia of the vascular endothelium.

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[15] Oliver, J.: Syphilitic Disease of the Thymus in Infants and the Mode of Origin of the DuBois Abscesses, Am. J. Dis. Child. **13**:158 (Feb.) 1917.

There is considerable difference of opinion regarding the relation of these extensive hemorrhages in the thymus and syphilis. Mendelsohn[10] and Schlesinger[9] maintain that there is an etiologic relation between thymus apoplexy and syphilis. Hart[2] and Dudgeon[18] deny that such relationship exists, while Hecker[17] and Simmonds[16] omit any reference to thymus hemorrhages in describing the histologic changes in the thymus in congenital syphilis. On the other hand, it is significant that in all the reported cases in which a detailed microscopic description is available (five cases) there was either a family history or anatomic changes that were either strongly suggestive or positively indicative of syphilis. In the other cases there were some with a specific history and others with nothing to suggest syphilis. Our cases undoubtedly have a syphilitic basis, yet we are unwilling to give the impression that extensive hemorrhages in the thymus are necessarily pathognomonic of syphilis.

The etiology of thymus apoplexy is obscure. So few cases have been reported and such varying causes have been ascribed that final judgment must wait on a larger number of thoroughly described cases. It is probable that one or more of four factors play a part in each case. Circulatory stasis as a cause, especially in a thymus the seat of marked hyperplasia is emphasized by Hart,[2] Klose[12] and Marfan.[5] When this is the main factor, the hemorrhage is diffused throughout the gland giving the appearance of a hemorrhagic infarct. A second factor is trauma, especially birth trauma, which is stressed by Weber, Friedleben, Raudnitz and Klose. The last author quotes Penkert and Veit as suggesting that thymus apoplexy is not an uncommon cause of death of new-born infants. A third factor is the presence of a hemor-

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16. Simmonds, M.: Die Thymus bei Kongenitaler Syphilis, Virchows Arch. f. path. Anat. **194:** (Suppl.) 213, 1908.

17. Hecker, R.: Beiträge zur Histologie und Pathologie der congenitalen Syphilis sowie zur normalen Anatomie des Fetus und Neugeborenen, Deutsch. Arch. f. klin. Med. **61:** 1, 1893.

18. Dudgeon, L. S.: A Contribution to the Pathology of the Thymus Gland, J. Path. & Bacteriol. **10:** 173, 1905.

rhagic disease of the new-born, that is, a defect in the coagulating mechanism of the blood such as occurred in both of our cases especially in the first one. This hemorrhagic tendency is frequently associated with if not due to, some underlying infectious process analogous to hemorrhages in the medulla of the suprarenal so commonly found in the new-born.[19] The fourth and probably the most important factor is the rôle played by infectious diseases, especially syphilis. It is very common to find small petechial hemorrhages in the thymus in infectious disease, in fact, Dudgeon noted them in 95 per cent. of the cases of pneumonia in infants. These minor hemorrhages are not to be confused with the more extensive blood extravasations referred to as thymus apoplexy in which the rôle of infection is not so clear. Undoubtedly, the hyperemia associated with an infection predisposes to hemorrhage. The fact that necrosis and suppuration preceded the hemorrhage in both of our cases makes the presence of an infection, probably syphilitic, most likely. Here, again, the same factor of infection plays the important rôle in hemorrhage in the suprarenal of the new-born.[19]

Another point of interest is that the early history of bleeding from the nose and mouth occurring in each of our cases indicated a hemorrhagic tendency and should have suggested appropriate serum or whole blood therapy to offset any complications, although with a syphilitic background, as in our cases, the results would have been the same.

The symptoms in our cases suggested a tendency to general hemorrhages, but there was nothing to indicate that the hemorrhage had involved the thymus gland. Nor have we found anything in the literature which would aid in the diagnosis of a thymus hemorrhage.

The possibility that the rapid enlargement of the thymus gland from the diffuse infiltration of blood could have been the immediate cause of death in a mechanical way cannot be excluded, especially in Case 2. The mechanical action of an enlarged thymus unassociated with other factors has been exaggerated and we do not feel that the evidence available justifies it as the cause of death in thymus apoplexy.

SUMMARY

Thymus apoplexy is a rare condition of extensive hemorrhage throughout the gland and is not to be confused with the smaller petechial hemorrhages frequently occurring in acute infections.

It usually occurs in very young infants or the new-born and is often associated with sudden death.

It seems to be associated with syphilis more than any other factor, but circulatory stasis, trauma, nonspecific infections and a hemorrhagic tendency are contributing, if not the main, factors in some cases.

There is no way of making a clinical diagnosis.

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19. Litzenberg, J. C., and White, S. M.: Hemorrhage in the Adrenal Glands of Infants, J. A. M. A. **51**:1964 (Dec. 5) 1908.

THE FOOD REQUIREMENTS OF CHILDREN

IV. CARBOHYDRATE REQUIREMENT

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NEW YORK

The carbohydrate in the diet of the growing child has, as far as is known, no specific function to perform. Nevertheless, it is a very essential component of the diet. It serves mainly as a source of energy, supplying the necessary calories which are not furnished by fat and protein. In so doing, however, carbohydrate accomplishes other purposes. It is the most efficient sparer of protein, being for this purpose superior to fat. This function of carbohydrate is so well known and has been so frequently discussed in the literature that it need not be taken up in detail here. It has been accepted generally that carbohydrate is essential for complete metabolism of fat, and that in the absence of carbohydrate from the diet, or when the amount is very low, fat is incompletely burned and acidosis may result.

When digestion is normal, a reasonable intake of carbohydrate is almost, if not quite, completely utilized in the body, leaving no residue to be eliminated in stools and urine. The excess that is not immediately used for energy is stored in the form of glycogen to be used later for energy or is converted into fat and added as such to the tissues of the body.

Carbohydrate is the most economical food from a physiologic as well as a commercial point of view. Physiologically, it is economical because of its complete utilization and because the energy required for digestion, that is, the "cost of digestion," is much lower than that of fat or protein. The commercial economy in carbohydrate foods is well known. They can be produced more cheaply than other foods; they can be stored for a long period without significant deterioration; they can be shipped and marketed in a compact form and are not readily affected by changes of temperature or by exposure. Because of these facts the market price of carbohydrate foods is much lower than that of the foods which are composed mainly of fat and protein. Table 1 gives the number of calories of carbohydrate which could be purchased for 10 cents at a small retail store in New York City, Feb. 1, 1922. For comparison are given the number of calories in fat and protein foods which could be purchased for the same amount at the same time and place.

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* Received for publication, March 17, 1922.

* From the laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital.

Carbohydrates form the greatest part of the diet of the human race at every period of life. The nursing infant receives a high proportion of carbohydrate as lactose in woman's milk, nearly one-half of the caloric value of the milk being due to the sugar. The nursing infant takes about 50 gm. lactose daily at the end of the first month and an average of 80 gm. daily during the latter part of the nursing period. Infants taking modifications of cow's milk usually receive more carbohydrate than do nursing infants. This is given because the amount of fat in modifications of cow's milk is in most cases considerably lower than that in woman's milk. Although a higher proportion of protein is given, this does not entirely make up for the reduction in the calories furnished as fat and consequently a larger amount of carbohydrate must be supplied.

TABLE 1.—Calories Purchasable for Ten Cents. Feb. 1, 1922

Articles	Retail Price	Number of Calories
Carbohydrate Foods:		
Sugar, granulated	6 cents per pound	3,100
Karo corn syrup	20 cents per 2.5 pound can	1,970
Oatmeal	12 cents per 20 ounce package	1,930
Rice	12 cents per pound	1,360
Bread	9 cents per 15 ounce loaf	1,270
Cream of wheat	30 cents per 28 ounce package	980
Potato	5 cents per pound	770
Jam	30 cents per pound jar	530
Fat Foods:		
Butter	49 cents per pound	740
Olive oil	65 cents per pint	600
Cream, Sheffield X (includes some protein and sugar)	32 cents per half pint	240
Protein Foods (include some fat):		
Cheese, American	35 cents per pound	590
Lean beef, round	44 cents per pound	200
Eggs, fresh brown	60 cents per dozen	180
Mixed Food:		
Milk, Sheffield, Grade A	18 cents per quart	355

The nursing infant receives carbohydrate entirely in the form of lactose. The infant on modifications of cow's milk may take lactose entirely or part lactose and part saccharose, maltose, dextrin, or starch, or a combination of these. It is not usual for any large proportion of the carbohydrate to be given as starch during the first year. When a mixed diet is taken at least one-half of the carbohydrate is usually in the form of starch, the rest being sugars—lactose, saccharose and fructose with occasionally a certain amount of dextrin and maltose.

The amount of carbohydrate taken by children more than 1 year of age varies according to the theories of the physician and the notions of the parent and even more according to the habits and tastes of the child. The carbohydrate variation is greater than that of any other constituent of the diet. Some children habitually take large amounts of bread, others live mainly on cereals, while with still others potatoes form the predominant article of diet. Many children consume an excessive amount of sugar, taking several teaspoonfuls on cereal and in other foods and sometimes even having sugar added to the milk taken. The relative amount of sugar taken by these children is steadily increased with age, since the child's palate demands a marked degree of sweetness in all foods and will not take those which do not taste sweet. In such cases the amount of sugar consumed soon forms a surprisingly large proportion of the diet to the exclusion of the other needed constituents.

Many children take, besides the amount of granulated sugar eaten with foods, a great deal in the form of jam, marmalade, jelly or syrup. It is often forgotten that syrup and honey are practically pure carbohydrate in a concentrated form, and that jam, marmalade and jelly usually contain from 80 to 90 per cent. sugar. Many a mother or physician who would think an ounce of granulated sugar excessive does not realize that an ounce of syrup or a rounded tablespoonful of jam contains practically the same amount of sugar. To these sources of carbohydrate must be added candy. There are few children who get no candy and the majority take several pieces and not a few as much as half a pound daily. A small piece of candy is equivalent to about one teaspoonful of sugar. It is obvious that a few pieces of candy increase the carbohydrate intake appreciably.

The degree to which sugar has come to form a prominent part of the diet of the American people is a cause for serious reflection. One hundred years ago the consumption of granulated sugar averaged only 8 pounds per capita. Last year the average was 84 pounds. The amount consumed as candy is a very large item in sugar consumption. The statement was made a few years ago by an official of a corporation operating 5 and 10 cent stores that their annual sales of candy exceeded 60,000 tons.

The carbohydrate intake of more than a hundred healthy children specially studied by us is shown in Charts 1 and 2. In Chart 1 are given the values in grams of the total carbohydrate taken daily. The curves shown are those representing the grams of carbohydrate which would be required to supply 50 per cent. of the total calories which are needed, according to our estimates,[1] at the different ages. Our investigations have shown that this proportion of the total calories, that is, 50 per cent., is the average taken as carbohydrate by a normal healthy child. The figures on which this average is based will be presented later.

In Chart 2 are given the values for the carbohydrate intake in grams per kilogram of body weight. The curves represent the grams of carbohydrate supplying 50 per cent. of the caloric requirement per kilo.

Charts 1 and 2 illustrate the wide variation in the carbohydrate intake of healthy children. This is most evident in the chart showing grams per kilogram. There are more very high values than very low ones and several instances of an intake of more than 15 gm. carbohydrate per kilogram. Chart 1 shows that there was more consistency in the total amount of carbohydrate taken daily. There are few low values, but several exceedingly high ones. One girl, 8 years of age, took 464 gm. carbohydrate daily. One boy, 9 years of age, took 560 gm.; another, aged 10, took 488 gm. and one, aged 14, took 683 gm. daily.

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[1] Holt, L. E., and Fales, H. L.: Am. J. Dis. Child. **21**:1 (Jan.) 1921.

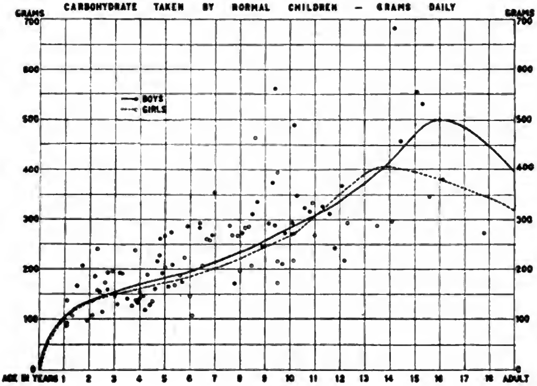

Chart 1

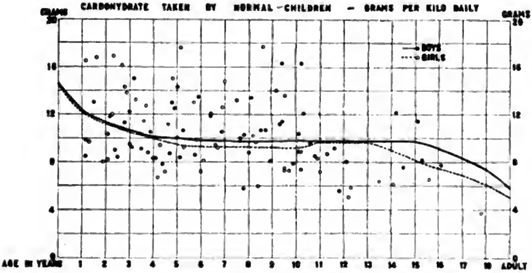

Chart 2

The average intake according to years is shown in Table 2, which gives the values for boys and girls separately and for both sexes grouped together. It will be seen that the total daily intake increases with fair regularity with the years, while the intake per kilogram decreases with the years. The average of all the cases, regardless of age, is about 10 gm. per kilogram. It is interesting to note that the carbohydrate intake per kilogram of the boys aged 14 to 16 showed a marked increase over that of the boys a little younger.

The observations reported in the literature, in which the carbohydrate intake of children after infancy was ascertained, show variations quite as wide as those in our own cases. As a rule, the amount of carbohydrate per kilogram of body weight taken by young children was higher than that taken by older children. The children studied by Müller [2] had very high intakes of carbohydrate, nearly all over 10 gm. per kilogram, while several children took as much as 17 gm. The intake of carbohydrate in Camerer's cases was low, as were the other constituents. Gephart [3] found that the amount of carbohydrate taken by the boys of St. Paul's School was much in excess of the average adult consumption, averaging more than 600 gm. daily. This represents an average of 13.7 gm. per kilogram for the youngest group of boys who averaged 13 years of age, 12.4 gm. per kilo for the group of boys who averaged 14½ years and 9.9 gm. for those averaging 16 years.

TABLE 2.—Average Carbohydrate Intake of Children. Original Observations

Age, Years	Boys			Girls			Both Sexes		
	No. of Cases	C-H Intake		No. of Cases	C-H Intake		No. of Cases	C-H Intake	
		Total Gm. Daily	Gm. per Kg.		Total Gm. Daily	Gm. per Kg.		Total Gm. Daily	Gm. per Kg.
1-2	2	90	9.2	5	154	12.8	7	128	11.8
2-3	4	142	10.0	7	179	13.3	11	165	12.1
3-4	6	147	10.9	4	176	11.7	10	158	11.2
4-5	7	178	10.2	5	166	9.4	12	173	9.8
5-6	5	219	11.1	5	211	11.9	10	215	11.5
6-7	3	280	11.5	5	196	9.3	8	228	10.1
7-8	2	261	10.3	3	274	11.2	5	260	10.8
8-9	4	291	10.8	5	288	10.5	9	289	10.6
9-10	5	357	12.2	4	247	8.9	9	308	10.7
10-11	6	338	10.9	3	272	8.5	9	317	10.2
11-12	3	292	7.8	1	268	7.2	4	286	7.7
12-13	1	366	8.0	2	257	5.5	3	293	6.3
13-14	..	...	....	1	287	6.4	1	287	6.4
14-15	2	571	9.9	1	296	6.2	3	480	8.9
15-16	2	541	9.6	1	346	6.6	3	476	8.1
16-17	1	380	7.8	..	...	....	1	380	7.8
17-18	..	...	....	1	272	4.8	1	272	4.8

The amount of carbohydrate in the usual adult dietary is from 400 to 550 gm. daily, which represents from 5 to 8 gm. per kilogram of body weight.

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[2] Müller, E.: Biochem. Ztschr. **5**:143, 1907.

[3] Gephart, F. C.: Boston M. & S. J. **176**:17, 1917.

Murlin[4] found that the men in the United States Army training camps took on the average 545 gm. carbohydrate daily. This is equivalent to 8.2 gm. per kilogram, the average weight being 146 pounds, or 66.5 kilograms.

From the data obtained concerning the diet taken by the normal children studied by us it was possible to calculate approximately the amounts of carbohydrate taken as sugar and as starch by these children. The values obtained are only approximate, since the relative amounts of sugar and starch used in cooking the various articles, such as cake, pudding, etc., could, in most cases, be only estimated from a knowledge of common recipés. It may be assumed, however, that our estimates are reasonably accurate.

It is surprising that the average of all the cases, regardless of age, showed that 51 per cent. of the carbohydrate intake was in some form of sugar. The proportion of sugar ranged from 27 to 82 per cent., but more than two-thirds of the values were between 40 and 60 per cent. In Chart 3 are given the proportions of starch and sugar taken by each child, arranged according to age. This shows that there is comparatively little individual variation in the distribution of the carbohydrate intake as starch and sugar. It is apparently usual in the mixed diet of children to give practically equal amounts of starch and sugar. It should be noted that the value for sugar includes not only the saccharose used in cooking or on cereals, etc., but also the fruit sugars and the lactose of the milk which was taken separately or which was used in the preparation of other foods.

TABLE 3.—Average Amounts of Starch and Sugar Taken

Age in Years	No. of Cases	Gm. Carbohydrate as		Age in Years	No. of Cases	Gm. Carbohydrate as	
		Starch	Sugar			Starch	Sugar
1-2	7	65	68	10-11	9	161	156
2-3	11	71	94	11-12	4	136	150
3-4	10	85	73	12-13	3	162	131
4-5	12	86	87	13-14	1	133	154
5-6	10	101	114	14-15	3	277	208
6-7	8	111	117	15-16	3	229	247
7-8	5	137	132	16-17	1	216	164
8-9	9	128	161	17-18	1	108	164
9-10	9	149	159				

Table 3 gives the average values according to years for the daily intake of starch and sugar.

It was also possible to estimate roughly the proportion of different sugars which made up the sugar intake. Some interesting observations were thus brought out. Table 4 shows the averages, according to years, of the grams of lactose, saccharose and fruit sugars taken by the children studied. It will be seen that the lactose intake does not vary

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[4] Murlin, J. R., and Hildebrandt, F. M.: Am. J. Physiol. **49**:531, 1919.

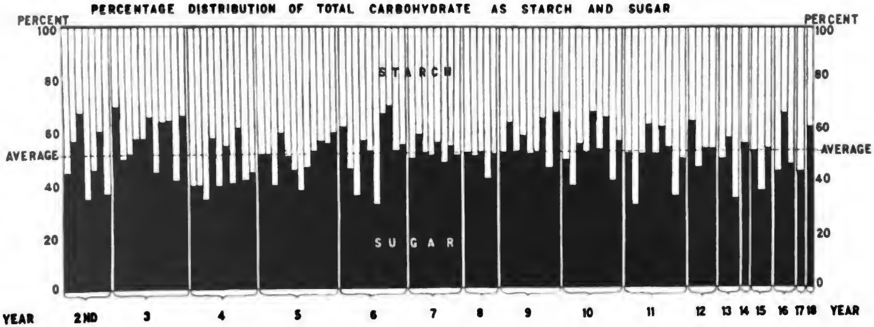

Chart 3

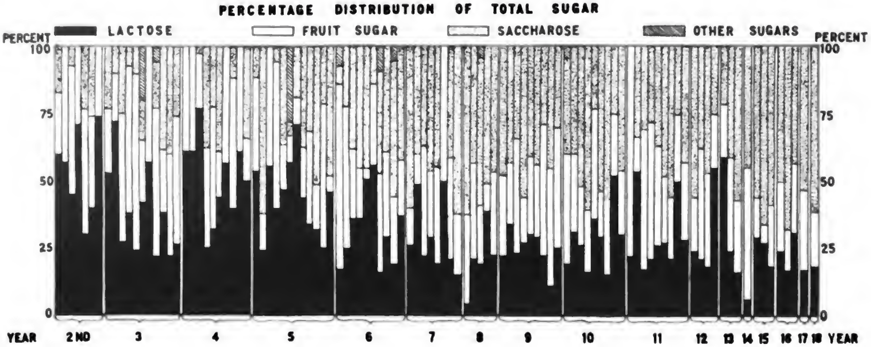

Chart 4

widely. The saccharose taken, however, shows an almost steady increase with age up to the eleventh year, with a marked increase during adolescence, the amount taken at that time being about ten times as much as the average taken by children under 4 years. It is surprising to note how much of the sugar was supplied by fruits. This value includes all the carbohydrate in the fruit. This is largely fructose but some of it is saccharose, and there is included in some instances a small amount of starch, for example, in apples and bananas when not thoroughly ripe.

In Chart 4 are shown the percentages of the total carbohydrate taken as different sugars by each child, the values being arranged according to age.

TABLE 4.—AVERAGE AMOUNTS OF DIFFERENT SUGARS TAKEN

Both Sexes.—Average Gm. Daily

Age, Years	No. of Cases	Lactose	Saccharose	Fruit Sugars*	Other Sugars	Total Sugars
1-2	7	30	9	24	..	63
2-3	11	33	19	40	2†	94
3-4	10	34	12	27	..	73
4-5	12	36	26	24	1‡	87
5-6	10	35	39	37	3§	114
6-7	8	29	55	33	..	117
7-8	5	24	69	38	1†	132
8-9	9	40	64	57	..	161
9-10	9	39	76	43	1†	159
10-11	9	44	53	59	..	156
11-12	4	42	59	44	5‡	150
12-13	3	48	48	35	..	131
13-14	1	9	69	76	..	154
14-15	3	48	124	31	..	203
15-16	3	55	140	52	..	247
16-17	1	27	87	50	..	164
17-18	1	29	102	33	..	164

* This includes all sugars occurring in fruit taken; largely fructose, but includes considerable saccharose and occasionally very small amounts of starch.
† Honey (levulose and dextrose).
‡ Maltose.
§ Honey and maltose.

The economic advantage of carbohydrate foods over fats and proteins has brought about a tendency to allow carbohydrate to form an excessive proportion of the modern diet. There are several important disadvantages in this procedure. The production of diabetes must be reckoned as a possible danger, as has recently been suggested.[5] If the proper caloric intake is maintained, a very high proportion of carbohydrate necessitates a low proportion of either fat or protein. Hence, there is a possible danger of reducing the amount of fat or protein below that which is necessary for normal nutrition. When a diet high in carbohydrate and low in fat and protein is taken, there may result an excessive retention of water in the tissues of the body. High carbohydrate feeding leads also to an excessive deposition of fat in the body. This condition is often seen in infants fed on sweetened condensed milk or on the proprietary foods, which are chiefly carbohydrate. It is quite usual with such feeding to achieve a rapid gain in weight. Infants fed in this way, however, are usually found to have very low resistance to infection. Their tissues are high in fat and water but low in muscle. When a digestive disturbance occurs, or when an infection takes place, this unnatural weight is rapidly lost and the child often succumbs readily. A similar condition was produced experimentally in pigs by Washburn and Jones.[6] They found that young pigs fed on sweetened condensed milk put on an excessive amount of fat. The protein increase in their bodies was, however, much below normal, and the bone development was defective, the bones being only two-thirds as strong as when whole milk was fed. Table 5 gives a summary of some of their findings.

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[5] Micheal, J. C.: Arch. Dermat. & Syph. **2**:455 (Oct.) 1920.

There is a growing belief that the large and constantly increasing proportion of carbohydrate in the diet of civilized races has a very important relation to the prevalence of dental caries. It has been observed that Arctic peoples, whose diet is almost entirely fat and protein with but very little carbohydrate—and that usually in the form of starch, rarely suffer from dental caries.

TABLE 5.—COMPARISON OF GROWTH IN SEVEN WEEKS OF SIX PIGS ON CONDENSED MILK WITH SIX PIGS ON WHOLE MILK

Feeding	Calorie Intake Daily	Weight, Gain in Kg.	Fat, per Cent. of Gain	Protein, per Cent. of Gain	Breaking Strength of Femur in Pounds
Whole milk	1,370	11.35	9.2	15.61	362
Sweetened condensed milk	1,270	8.10	23.65	10.92	243

Whole milk contained fat, 3.3; sugar, 5.2; protein, 3.6 per cent.
Sweetened condensed milk contained fat, 1.6; sugar, 9.8; protein, 1.6 per cent.

Stefansson, the Arctic explorer, has stated that he himself has examined 500 skulls which were dug up from an old cemetery in Iceland of about the eleventh century. In only one skull was an imperfect tooth found and that was evidently the result of injury. He further stated that the Eskimos who live on a meat diet have perfect teeth, but, when they come in contact with civilization and eat the foods of other races they suffer severely from dental caries.

Furthermore, archeologic researches have shown that dental caries was prevalent in ancient Egypt. More recently the discovery of a very primitive human skull in Rhodesia has shown that dental caries existed in earliest times. Both of these localities are tropical or subtropical in climate and the early diet was probably composed largely of plant foods and hence was predominantly a carbohydrate diet, a complete contrast to that taken by the Arctic peoples.

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[6] Washburn, R. M., and Jones, C. H.: Vermont Agric. Exper. Sta. Bull. 195.

Whether the tendency to dental caries is due to an excess of carbohydrate or to a consequent reduction of other constituents of the diet—fat, protein, mineral salts or vitamins—has not yet been established.

Of great importance, also, is the effect on digestion of a diet in which the proportion of carbohydrate is excessive. When a very large amount of carbohydrate, especially in the form of sugar, is taken into the digestive tract at one time, it is often impossible for absorption to take care of it. The consequence of this is excessive fermentation in the intestine, due to bacterial action, with the formation of carbon dioxid and organic acids, which may be very irritating to the mucous membrane of the intestine. This excess of acid usually causes a quickened peristalsis with large, loose, acid stools. The result is a decreased absorption of all the food constituents and frequently a serious diarrhea. When the diet contains an excess of carbohydrate in the form of starch, somewhat different symptoms frequently develop. There is often constipation, great abdominal distention, flatulence and colic.

TABLE 6.—GRAMS OF CARBOHYDRATE COMBINED WITH ONE GRAM VEGETABLE PROTEIN

Food	Gm. Carbohydrate per Gm. Protein	Food	Gm. Carbohydrate per Gm. Protein
Peanut butter	0.6	Bread	5.8
Soy beans	0.6	Rice	6.4
Walnuts	0.7	Cream of wheat	6.9
Peas	2.4	Potatoes	8.4
Lima beans	3.7	Carrots	8.4
Oatmeal	4.2		

Usually these disorders of digestion are acute and not very severe, yielding quickly to proper dietetic treatment. When, however, they are frequently repeated or are prolonged through lack of proper dietary adjustment, they lead to serious chronic disturbances with marked loss in weight. This condition is often difficult to control and a very great reduction in the carbohydrate of the diet is required for a long time before the normal tolerance for carbohydrate is reestablished. This condition is most frequently seen in the second and third years of life.

In the discussion of the protein requirement of the child we have stated that if vegetable proteins are depended on to supply the protein need during growth very large amounts of carbohydrate are inevitably given, since vegetable proteins occur only in combination with large amounts of starch. Table 6 shows the amount of carbohydrate, usually in the form of starch, which is combined and necessarily given with each gram of vegetable protein in some common foods. It will be seen from this table that nuts and soy beans are the only foods which supply much vegetable protein without including very large amounts of carbohydrate.

Although nuts have been found to be well utilized by adults without disturbance of digestion, the wisdom of giving them to children in any considerable quantity is questionable. It is not advisable to depend on them as a source of protein. It would appear from its chemical composition that the soy bean is an excellent source of vegetable protein. This vegetable, used so extensively in China, is not familiar to the American people. It has a peculiar flavor, not very palatable according to our tastes, and on that account will probably not gain any great popularity in this country, where other sources of protein are readily available.

In the other articles of food which supply vegetable protein there is so much carbohydrate combined with the protein that there is danger of serious disturbance of digestion from the excess of carbohydrate. It is evident that for this reason alone, as well as for the others given in a preceding article, it is not wise to depend on vegetable foods to supply the protein need of the child.

As has already been stated, in addition to the positive harm which may follow excessive use of carbohydrate in the diet of the child, there must always be considered the additional disadvantage which follows this plan of feeding because of the inevitable reduction of fat and protein.

It has been shown that a definite amount of protein should be included in the diet of the growing child.[7] It seems rational to allow in the diet at least as much fat as protein.[8] The total calories needed at any age can be estimated with a fair degree of accuracy.[1] Hence, the amount of carbohydrate required is determined by subtracting from the total caloric need the calories supplied by the needed amounts of fat and protein. On this basis there should be allowed for the healthy child of average activity about 12 gm. carbohydrate per kilogram at 1 year, decreasing to between 9 and 10 gm. or about 1 per cent. of the body weight, at 6 years and maintaining about this value throughout the remainder of the growth period.

If the total caloric need is raised above the average by increased muscular activity, carbohydrate may be used to provide the entire amount of extra energy, since an increase in muscular activity does not increase the needs in protein or fat above the normal.

SUMMARY

1. Carbohydrate is a desirable and probably an essential component of the diet, although it does not have any specific function in nutrition. It forms the largest part of the diet at all periods of life.

2. Nursing infants take on the average about 12 gm. carbohydrate per kilogram of body weight daily. Artificially fed infants usually receive somewhat more than this.

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[7] Holt, L. E., and Fales, H. L.: Am. J. Dis. Child. **22**:371 (Oct.) 1921.

[8] Holt, L. E., and Fales, H. L.: Am. J. Dis. Child., to be published.

3. The carbohydrate in the diet of the infant is almost all sugar, that of the nursing infant entirely lactose, that of the artificially fed infant usually a mixture of lactose with saccharose or maltose and dextrins.

4. The carbohydrate intake of more than one hundred healthy children from 1 to 18 years of age, studied by us, averaged 10 gm. per kilogram. Of this 51 per cent. was sugar, including lactose, saccharose and fructose, and 49 per cent. was starch.

5. Carbohydrate is more economical than fat or protein, both physiologically and commercially. Because of this latter advantage there is a growing tendency to increase the proportion of carbohydrate in the diet beyond the amount which is desirable.

6. When a very large proportion of the food is in the form of carbohydrate, the intake of fat or of protein or of both is likely to be less than the normal nutritive need of the body.

7. A diet excessive in carbohydrate leads to an abnormal deposition of fat without a corresponding increase in muscle development. Children taking such a diet have feeble resistance to infection.

8. There is evidence that a relationship exists between the high proportion of carbohydrate in the modern diet and the prevalence of dental caries.

9. Definite digestive disturbances, chiefly intestinal, may be produced when the carbohydrate in the diet is excessive. There may result increased fermentation with loose acid stools or constipation with flatulence and abdominal distention. When long continued these disturbances are very difficult to control.

10. Carbohydrate furnishes the calories needed in the diet which are not supplied by the requisite amounts of fat and protein.

11. It seems rational to allow in the diet of the child of average activity about 12 gm. carbohydrate per kilogram of body weight at one year, decreasing the amount to about 10 gm. per kilogram at 6 years and maintaining it at this value throughout the remainder of the growth period.

12. An increase in the total caloric need because of increased activity may be supplied by carbohydrate alone.

FOOD REQUIREMENTS IN NEW-BORN INFANTS

A STUDY OF THE SPONTANEOUS INTAKE

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Food requirements are commonly estimated by one of two methods, by measuring the heat output or by measuring the caloric intake. Heat output, as measured by direct or indirect calorimetry, has been most useful and has given the most significant information in defining our standards of basal metabolism. Such information as we have on the total energy requirement has come, in the main, from measurements of the total food intake. In the new-born this has been determined from the amounts of breast milk taken by healthy infants. The summary of von Reuss,[1] condensed in Table 1 and plotted in Figure 1, includes most of the data in the literature covering this point.

There is, however, a serious objection to figures based on an assumed correspondence between intake and needs. The amount of breast milk obtained is governed by the supply available. That the supply during the first few days is not adequate has been proved by metabolic measurements and by clinical observation. Thus Benedict and Talbot [2] state, on the basis of their observations, that "even under the most favorable conditions the total amount of available energy in the colostrum which the child receives from the mother's breast during the first few days is wholly insufficient to supply the energy needs, even when we consider only the basal metabolism. Still less does this scant fuel supply serve for the probable increment above basal metabolism caused by the restlessness, crying and varied muscular activity of the infant throughout the day. It is thus seen that the struggle for existence and struggle for food begin simultaneously with the new-born infant. Since the food supply is so obviously insufficient, we may ask why nature does not provide more liberally during the first few days. It is a most striking fact that only human mothers and new-born infants are so entirely dependent on the care of others. The relationship between this fact and the development of civilization is most interesting and leads one to ask if this scant food supply is a natural consequence of civilization." The not infrequent occurrence of inanition fever dur-

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* Received for publication, June 15, 1921.

* From the Division of Pediatrics, Stanford University Medical School.

1. Von Reuss, A. R.: Die Krankheiten des Neugeborenen, J. Springer, Berlin, 1914, pp. 91, 92.

2. Benedict, F. G., and Talbot, F. B.: The Physiology of the New-Born Infant, Carnegie Institution of Washington, Pub. No. 233, Washington, D. C., 1915, pp. 124-126.

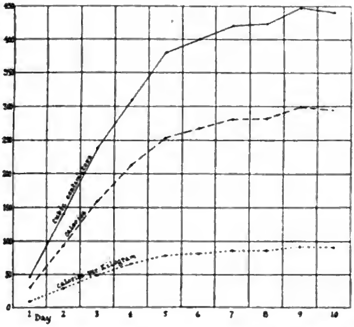

Fig. 1.—Average normal intake of breast milk. Calculated from von Reuss' compilation.

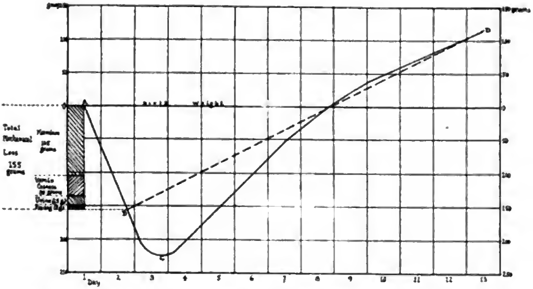

Fig. 2.—Line ACD: actual weight curve—average of 112 infants. Line ABD: theoretical ideal weight curve.

ing the first few days is direct evidence that the water supply, at least, is inadequate and it can be readily shown (Fig. 2) that the initial loss even of the most favored group of so-called normal babies far exceeds the mechanical loss. The respiratory quotient shows that during the first days the metabolic processes rapidly exhaust the stored carbohydrate and soon attack the stored fat and sometimes perhaps the body protein. Acidosis at this time is not uncommon.[2]

If we wish to know something more about the total needs for food during these first days of life we can adopt another procedure; we may offer the infant all the food which he desires and determine the amounts which he actually takes in the presence of plenty. So far as I can find no one, except Murlin and Bailey,[3] has attempted feeding of this sort in the new-born, and their results are not reported in detail.

TABLE 1.—Summary of Cases Showing Breast Milk Intake for First Ten Days of Life *

Day	Number Cases	Average C.c. Breast Milk	Average Calories	Average Energy Quotient	Average Weight, Gm.
1	109	46	31	9	3,250
2	155	140	93	29	
3	157	238	159	49	
4	175	319	213	66	
5	177	380	253	78	
6	179	401	267	82	
7	170	421	281	87	
8	161	423	282	87	
9	147	448	299	92	
10	64	442	295	91	
Seven Cases (Feer)					
1	...	4	3	1	3,578
2	...	50	33	10	
3	...	177	118	37	
4	...	315	210	67	
5	...	456	304	98	
6	...	549	366	116	
7	...	552	368	117	
8	...	567	378	120	
9	...	562	375	119	
10	...	603	402	127	

* From von Reuss' compilation. The original sources were in some instances consulted.

For reasons, into which it is not necessary to go fully, about ninety new-born infants in the wards of Lane Hospital were fed in this way. The infants were put to the breast every four hours, an effort being made to obtain for them all the breast milk available, and then given as much of one of the formulas to be described as they wished to take. By weighing before and after nursing and by measuring the quantities taken from the bottle, the total intake was determined. In all, about eighty-five records were complete enough for statistical analysis, making a total of 932 patient days or 5,592 feedings. By using the average figures of Holt, Courtney and Fales[4] for colostrum milk, of Van Slyke[5] for cow's milk, and of an analysis of Red Label Karo Syrup made for me by Dr. F. J. Cajori of Stanford University, the caloric values of the ingested food were determined. The variability in composition, especially of colostrum is fully recognized. This would not seriously invalidate the averages for the whole group and would only emphasize the importance of individual variation, of which a special point will be made.

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[3] Bailey, H. C., and Murlin, J. R.: The Energy Requirement of the New-Born, Am. J. Obst. **71**:526, 1915.

During the first twenty-four hours all infants were offered 15 per cent. Karo solution with a caloric value of about 620 calories per liter. Thereafter they were offered after nursing one of the formulas shown in Table 2. These formulas were based on Pirquet's conception of an "equivalent milk"[6]—a mixture having approximately the same caloric value as whole milk. Fear of disorders from butter fat led to the use of a low fat percentage. The use of corn syrup, introduced in pediatrics by Marriott[7]—a highly hydrolyzed starch, consisting of dextrose and its polymers—seems logical. In our experience, practically no disturbance of digestion has followed the use of the rather high carbohydrate mixtures. Having been brought to a boil at the time of preparation, these were practically sterile.

TABLE 2.—GENERAL FORMULA

Certified milk	400 C.c.
Karo corn syrup (red label)	120 C.c.
1 per cent. barley water	480 C.c.

Mix and bring to a boil.

Formula 1: with whole milk
Formula 2: with skimmed milk, taking the top 4 ounces from the quart
Formula 3: with skimmed milk, taking the top 7 ounces from the quart

	Composition			
	Fat	Carbohydrate	Protein	Cal. per Liter
Formula 2	0.6	14.0	1.3	679
Formula 3	0.3	14.0	1.3	653
Colostrum*	2.8	7.6	2.3	667
Cow's milk†	3.9	5.1	3.2	698

	Composition of Karo (Red Label)	
	Per 100 Grams	Per 100 C.c.
Water	22.96 Gm.	32.1 Gm.
Ash	1.36	1.9
Soluble carbohydrates	75.37	105.0
Sucrose	1.3	1.8
Maltose	6.0	8.4
Glucose	24.4	34.0
Dextrins	43.8	61.0
Specific gravity, 1.393		

* Analyses of Holt, Courtney and Fales.
† Analyses compiled by Van Slyke.

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4. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**: 229 (Sept.) 1915.

5. Van Slyke, L. L.: Modern Methods of Testing Milk and Milk Products, The Orange Judd Company, 1915, pp. 15-16.

6. Von Pirquet, C. F.: System der Ernährung, J. Springer, Berlin, 1917.

7. Marriott, W. McK.: The Artificial Feeding of Athreptic Infants, J. A. M. A. **73**:1173 (Oct. 18) 1919.

Average Intake.—Table 3 and Figure 3 show the total average fluid intake and caloric intake. The total intake rises rapidly in a smooth curve to the fifth day and then increases more slowly and somewhat irregularly to a maximum of about 600 c.c. and 400 calories on the twelfth day. Reduced to cubic centimeters and calories per kilogram, as in Figure 4 and Table 4, the intake will be seen to increase rapidly to about 150 c.c. and 100 calories on the fifth day, after which it rises more slowly and irregularly to about 160 c.c. and 115 calories on the twelfth day. In Figure 5 the relation of the caloric intake to previously established standards is shown. On the second day, the intake equals the basal needs, as determined by Benedict and Talbot; on the third day, it slightly exceeds the total average requirement of these investigators; on the fifth day, it equals the average total requirement of Heubner,[8] above which it rises slightly during the succeeding days. It should be noted here that the estimates of Benedict and Talbot do not

TABLE 3.—Total Intake

Day	No. Cases	Average Weight, Gm.	Average Gain or Loss, Gm.	Average Total Fluids, C.c.	Average Total Calories
1	87	3,350	.....	104	69
2	86	3,226	—124	217	145
3	86	3,204	— 22	315	210
4	85	3,225	+ 21	409	272
5	85	3,268	+ 37	453	301
6	87	3,298	+ 30	483	322
7	84	3,338	+ 40	515	343
8	84	3,370	+ 32	518	345
9	84	3,392	+ 22	508	338
10	82	3,413	+ 21	525	350
11	69	3,431	+ 18	556	270
12	13	3,463	+ 32	586	290

TABLE 4.—Average Intake in Cubic Centimeters and Calories Per Kilogram

Day	No. Cases	Average C.c. per Kilo	Average Calories per Kilo
1	87	34.4	22.5
2	86	68.1	48.1
3	86	98.6	68.8
4	85	124.9	89.6
5	85	137.9	98.9
6	87	144.4	104.1
7	84	152.7	107.9
8	84	150.7	108.2
9	84	147.6*	104.2
10	82	154.5	111.0
11	69	157.2	114.6
12	13	167.3	117.3
5-12	588	149.3	105.3

* The slightly lower intake here is probably due to the fact that a number of infants were circumcised at this time.

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[8] Heubner, O., and Heubner, W.: Zur Lehre von der energetischen Bestimmung des Nährungsbedarfes beim Säugling, Jahrb. f. Kinderh. **72**:121, 1910.

include an allowance for growth. The quantities of breast milk in the present series cannot be regarded as normal. There is definite reason for believing that the breast milk supply of the mothers in our wards has for several years been diminishing steadily (Fig. 6), and, in fact, this was the real reason for undertaking the present experiment. It is of interest to note that the breast milk supply did not until the sixth day touch the level of basal requirements and had not by the twelfth day attained the level of total average requirements minus the growth quota.

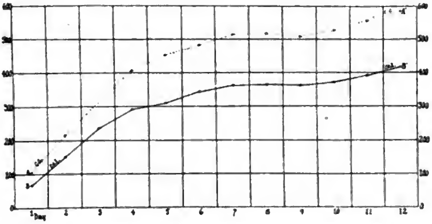

Fig. 3.—Line A-A': average daily intake in cubic centimeters. Line B-B': average daily intake in calories.

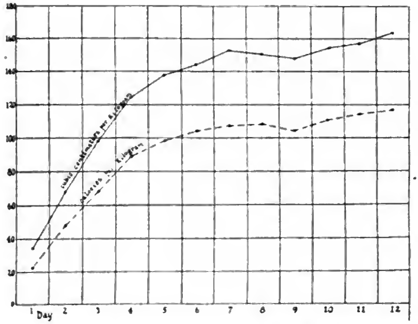

Fig. 4.—Total intake in cubic centimeters and calories per kilogram.

Figure 7 and Table 5 show the relation of the spontaneous intake in the present series to the average breast milk supply in von Reuss' compilation and to Feer's[9] series of seven cases in which the milk supply was especially abundant and the infants made particularly rapid progress in weight. It will be seen that for the entire breast milk series, the caloric intake is 10 or 15 calories per kilogram lower, but that in Feer's series after the fifth day the breast milk intake was 5 or 10 calories greater than in the present series. It is noted in most of the cases in von Reuss' compilation that the infants had failed to regain birth weight at the time of last observation. Figure 7 shows clearly that during the first four days, in so-called normal cases, the breast milk intake is less than the average total requirement, and even in the case of babies whose mothers have an unusually abundant supply of breast milk, the supply does not measure up to appetite until the sixth day.

Rate of Gain.—Figure 2 attempts to show what may be regarded as the ideal weight curve, compared with the actual curve of the most favored group of babies to be found in our earlier records. (The two curves were constructed before the present feeding experiment was begun.) . The initial loss in the actual curve was approximately 225 gm., while the average mechanical loss (taken, in the main, from the figures of Griffith and Gittings[10]) is only about 155 gm. Regarding the latter as the ideal average loss, and assigning the average daily gain found in normal babies for the first month, a hypothetical curve is obtained which may be considered as the ideal for the first twelve days. It will be seen that supposedly normal babies with the natural breast milk supply lose about 225 gm. during the first two days, then and up to the eighth day they gain at a very rapid pace; at this time they reach the ideal level and thereafter gain at the usual rate. Figure 6 shows the average rate of gain of three unselected series of babies from three earlier periods in our wards as compared with the ideal curve, and, to the right, the incidence of inanition fever in the same

TABLE 5.—ENERGY QUOTIENT OF PRESENT SERIES COMPARED WITH THAT OF FEER'S SEVEN CASES AND VON REUSS' COMPILATION

Day	Present Series	Feer's Series	von Reuss' Compilation
1	23	1	9
2	48	10	29
3	69	37	49
4	90	67	64
5	99	96	78
6	104	116	82
7	108	117	87
8	108	120	87
9	104	119	92
10	111	127	91

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[9] From von Reuss, loc. cit.

[10] Griffith, J. P. C., and Gittings, J. C.: The Weight of Breast-Fed Infants During the First Two Weeks of Life, Arch. Pediat. **24**:321, 1907.

series. Figure 8 shows the composite average of the three earlier periods as compared with the ideal and with the present series. It will be seen that the curve of the present series and of the ideal are practically identical. At the right is shown the incidence of inanition fever for all the series. Actually, one case developed in the present series; this, in a baby who refused all food and who recovered only when fed by gavage. From this figure, it appears that the average intake as determined by appetite closely corresponds with the average amount required to sustain an ideal curve of weight.

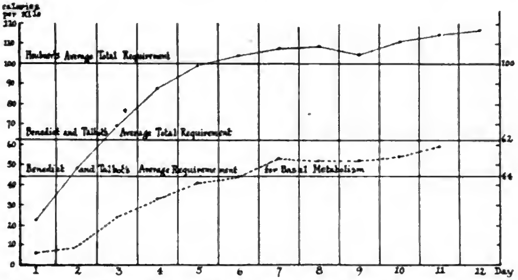

Fig. 5.—Spontaneous intake of food by new-born infants in calories per kilogram. Average of entire group. Solid line: total intake; broken line: breast milk.

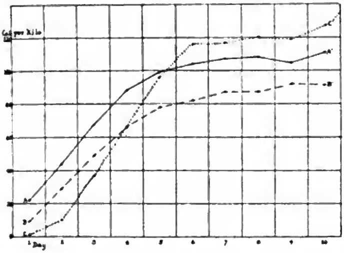

Fig. 6.—Average weight curves of three earlier periods contrasted with ideal curve.

Figure 9 shows the average daily total gain plotted against the average daily total intake, from the time of low weight following the initial loss to the time of dismissal, or, as a rule, from the third to

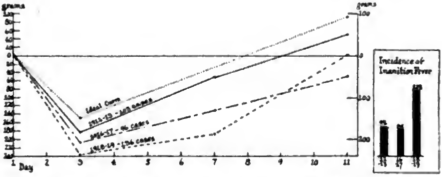

Fig. 7.—Spontaneous intake in calories per kilogram. Solid line: present series (A-A′); broken line: average nursing infant (B-B′); dotted line: Feer's seven cases (C-C′).

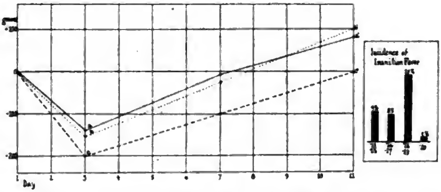

Fig. 8.—Weight curve of present series contrasted with earlier series and with ideal curve. Line a-a′: present series; line b-b′: theoretical ideal; line c-c′: average of three earlier series.

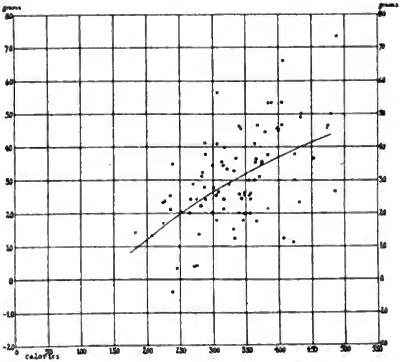

Fig. 9.—Average daily gain referred to average daily caloric intake.

the eleventh day. It shows that a satisfactory gain cannot be assured on less than 300 calories daily, and that in general, the average rate of gain follows the total caloric intake. Very striking, however, is the variability; the scatter of the graph is very wide; the proportion of calories retained for growth varies prodigiously in different infants. Figure 10 reduces the same data to calories per kilogram and gain to percentages of the body weight. The variability here also is striking. It will be noted that the average daily gain is 0.9 per cent. of the body weight daily, or 9 gm. per kilogram and the intake almost exactly 100 calories per kilogram daily. The greatest concentration of measures lies between 0.57 and 1.24 per cent. of the body weight daily for gain, and between 88.5 and 110 calories per kilogram per day for intake.

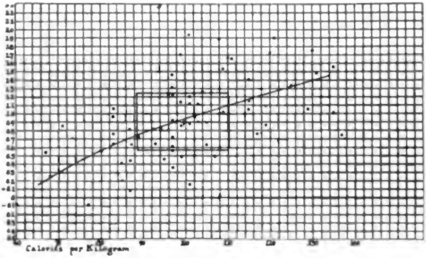

Fig. 10.—Average daily gain or loss in percentage of body weight referred to average daily caloric intake; period from third day to time of dismissal.

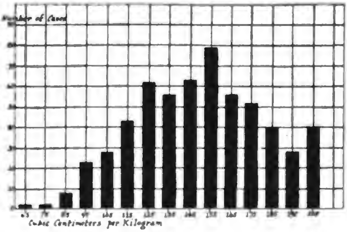

Fig. 11.—Distribution of Fluid Intakes in cubic centimeters per kilogram. Period from fifth to twelfth day inclusive.

Variability.—Averages at best show general tendencies; they have little bearing on the individual case unless something is known of the variability from the average of the individual components of the group. To measure variability certain mathematical methods, based on the frequency distribution, have been much used of late in the study of clinical statistics. For the purposes of the present study two frequency graphs (Figs. 11 and 12) have been made, showing the distribution of fluid intake and of energy quotient for the period from the fifth day—at which time the intake first reaches a plateau—to the time of last observation on the eleventh and twelfth days. A few infants are found who take as little as 65 and 75 c.c. per kilogram daily; for each increment of 10 c.c. the frequency increases until at 155 c.c. daily per kilogram we find the greatest number of cases. This point is the mode, or point of maximum frequency of the curve and corresponds approximately with the average. With further increments of quantity, the number of cases, or frequency, diminishes, but even at 205 c.c. per kilogram we find a considerable number of cases. It is obvious that while the largest number of infants take 15.5 per cent. of their body weight daily during the period between the fifth and twelfth day, the extreme range of variation lies between 6.5 per cent. and 20.5 per cent. of the bodyweight. Likewise, in the case of calories per kilogram, while the greatest number of infants for the period took 105 calories per kilogram the range was between 45 and 195 calories. This is the extreme range. In order to separate the certainly normal from the possibly abnormal, I have suggested in another paper[11] that the stand-

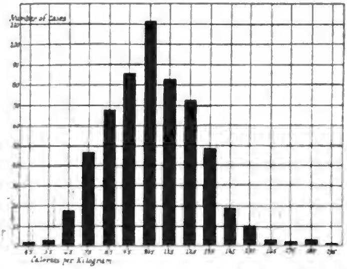

Fig. 12.—Distribution of Caloric Intakes in Calories per kilogram. Period from fifth to twelfth day inclusive.

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[11] Faber, H. K., and James, C. A.: The Range and Distribution of Blood Pressures in Normal Children and the Clinical Application of Statistical Methods to the Interpretation of Deviations from the Normal Average. (To be published in the Am. J. Dis. Child.)

ard deviation[6] of Pearson be used. Measuring off the standard deviation above and below the mean or average we find the range of certainly normal, which will include about two-thirds of the cases in most clinical statistics. We may still further restrict our range to the central 50 per cent. of cases by the use of the so-called probable error. This has certain convenient practical implications. For the period from the fifth to the twelfth day inclusive, the probable error—the variation in either direction from the mean—is 15.9 calories per kilogram and 21.3 c.c. per kilogram. The variation is, therefore, ± 15.1 per cent. for calories and ± 14.3 per cent. for fluid intake per kilogram. The range of variation of the 50 per cent. of cases nearest the average is shown for each day in Figures 13 and 14. As an example of the degree of variation it will be noted, that on the tenth day, while the average intake

TABLE 6.—VARIABILITY IN INTAKE

Day	No. Cases	Calories per Kilogram			C.c. per Kilogram		
		Average Intake, Calories	Average Variation, Calories*	Average Variation, %	Average Intake, C.c.	Average Variation, C.c	Average Variation, %
1	87	22.5	9.2	40.9	34.4	14.7	42.7
2	86	68.8	14.4	29.9	68.1	19.6	28.8
3	86	68.8	13.1	19.0	98.6	19.5	19.8
4	85	89.6	16.3	18.2	124.9	22.9	18.3
5	85	98.9	15.7	15.9	137.9	22.4	16.2
6	87	104.1	16.7	16.0	144.4	22.6	15.7
7	84	107.9	16.4	15.2	152.7	20.5	13.4
8	84	108.2	16.2	15.0	150.7	21.6	14.3
9	84	104.2	13.7	13.1	147.6	19.0	12.9
10	82	111.0	15.0	13.5	154.5	20.0	12.9
11	69	114.6	15.7	13.7	157.2	19.0	12.1
12	13	117.3	9.6	8.2	167.3	15.1	9.0
5-12	588	105.3	15.9	15.1	149.3	21.3	14.3

* More strictly, the "probable error," which marks the limits above and below the average within which half the cases will occur. The other half will vary more than this amount from the average.

TABLE 7.—COMPARISON OF QUANTITY OF BREAST MILK OBTAINED BY INFANTS IN TWO SERIES

Day	Number of Cases		Average C.c. Breast Milk		Average Calories		Average Calories per Kilo		Average Gain or Loss		Average Birth Weight	
	First Series	Second Series	First Series	Second Series	First Series	Second Series	First Series	Second Series	First Series	Second Series	First Series	Second Series
1	4	3	31	20	21	13	6	4	....	...	3,350	3,312
2	83	60	43	43	29	29	9	9	—124	—115		
3	85	63	115	123	77	82	24	26	—22	—47		
4	83	65	183	191	122	128	38	44	+21	+21		
5	83	58	228	260	152	174	46	55	+37	+15		
6	84	58	237	277	158	185	48	58	+30	+30		
7	82	58	265	309	177	206	53	64	+40	+ 9		
8	82	56	263	315	175	210	52	65	+32	+ 8		
9	82	57	263	335	175	223	52	69	+22	— 5		
10	79	60	277	346	185	231	64	72	+21	+10		
11	65	54	300	334	200	223	58	69	+18	+16		

First series: Infants with unlimited complementary feeding.
Second series: Infants given complementary feeding only when breast milk was less than 100 c.c. per kilogram, or 67 calories per kilogram.

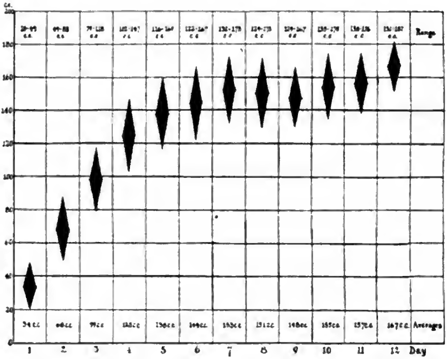

Fig. 13.—Daily fluid intake in cubic centimeters per kilogram body weight showing range of variation of 50 per cent. of the cases.

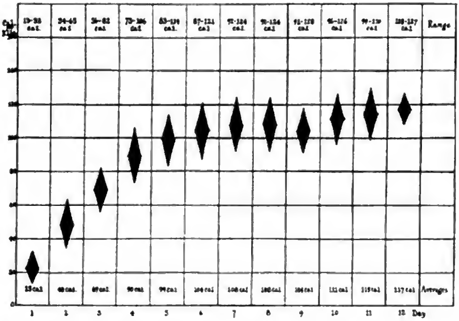

Fig. 14.—Daily intake in calories per kilogram body weight showing range of variation of 50 per cent. of the cases (± P.E.).

amounts to 111 calories per kilogram, the range of the central half of the cases extends from 96 to 126 calories. The complete figures are given in Table 6.

Since Benedict and Talbot estimate that the average total requirement of new-born infants is about 62 calories per kilogram, and since in the series here reported the spontaneous intake rose to this point on the third day and to 115 calories on the eleventh day, the question arose whether these infants were not actually taking more than they needed. Unlimited feeding was accordingly dropped, except for the first twenty-four hours; and a plan initiated by which each infant was assured at least 100 c.c. of breast milk or equivalent formula per kilogram daily. No infant taking this amount or more of breast milk was given complementary feeding. He was thus assured about 67 calories per kilogram and any excess over this was supplied by breast milk alone. The records of sixty-two babies so fed are complete enough for analysis. The data are presented in Figure 15 and in Table 7. It will be seen that these infants obtained a little more breast milk but that the weight curve was unsatisfactory after the initial loss. That the latter was the same as for the first series was probably due to the fact that 15 per cent. Karo solution was used in the same way during the first day in both series.

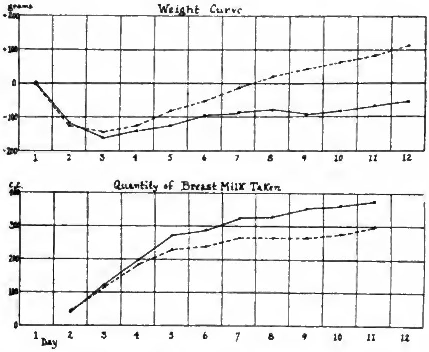

Fig. 15.—Solid line: average of babies on breast milk alone or with limited complementary feeding. Broken line: average of babies with unlimited complementary feeding.

COMMENT

This paper does not deal with the question of whether or not a low or inadequate intake of food during the early days of life is a useful natural provision for increasing the vigor of sucking and hence for increasing the supply of breast milk. Nor does it advocate the method of feeding employed. Its only present purpose is to show the intake of food, as energy, when the appetite of the infant is the only controlling factor, and to relate the values found with weight and rate of gain, and with the values previously determined by other methods.

As a result of the metabolic measurements of Benedict and Talbot there is at present a sharp divergence of opinion as to the caloric requirements of new-born infants. The discrepancy is more apparent than real. The measurements by these investigators show a basal rate of about 44 calories per kilogram and an estimated average total metabolism, exclusive of growth, of about 62 calories. To this figure about 15 calories[12] may properly be added as the average quota of calories retained for growth, making a total of about 77 calories per kilogram per day.

On the other hand, Heubner's figure of 100 calories as the average optimum intake has obtained abundant clinical corroboration. Beck (quoted by Morse and Talbot[14]), compiling the average breast milk intake from the literature, found, for instance, that from 1 to 12 weeks the average intake is 107 calories per kilogram. The intake figures for the first week are, as a rule, lower, and a few cases of apparently normal progress have been reported on 50 calories or less (averaged for the week). As above stated, however, the extent of the initial loss commonly regarded as normal is greater than the mechanical loss, and the figures given measure supply rather than demand.

Benedict and Talbot's figures are for the first seven days and deal with babies receiving either no complementary feeding or only small amounts of very dilute formulas. Unfortunately, they did not measure the caloric intake. The average age of the 105 infants in their series is about 2 days, 16½ hours. They found that from the second to the seventh day the minimum heat production was fairly stable.

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[12] Pfaundler and Schlossmann: Handbuch der Kinderheilkunde, Edit. 2, F. C. W. Vogel, Leipzig **1**:183, 1910. Here will be found Camerer and Söldner's Chemical Analysis of Six New-Born Infants. The growth quota I have calculated from this analysis (fat, 12.3 per cent.; protein, 11.7 per cent.; extractives, 1.5 per cent.; estimating extractives as carbohydrate) and from the average 9 gm. found in the present series as the daily increment per kilogram body weight. The value is in fair agreement with Camerer's[13] figure of 15 per cent. and with Rubner and Heubner's[13] figure of 12.2 per cent. of the total calories as the retention for growth.

[13] Quoted from Lusk, G.: The Elements of the Science of Nutrition, Ed. 3, W. B. Saunders and Company, Philadelphia and London, 1917, p. 412.

[14] Morse, J. L., and Talbot, F. B.: Diseases of Nutrition and Infant Feeding, Ed. 2, The Macmillan Company, New York, 1920, p. 73.

In the present series the average total caloric intake for the period from the second to the sixth day inclusive was 82 calories per kilogram; or, to compare the data more accurately with the Benedict and Talbot figures, the average intake from the first to the seventh day inclusive, was 77.3 calories. This is in almost exact agreement with the Benedict and Talbot estimate when 15 calories are added to the latter for growth.

During the second week the correspondence with the figures of Benedict and Talbot no longer holds. The average intake from the eighth to the twelfth days inclusive in the present series was about 107 calories per kilogram, which is in exact agreement with the results of Beck's compilation.

It would naturally be erroneous to regard the average for the first week as applying to each day of that week. Calorimetry and food measurement both assign a low value to the energy requirement on the first day. During the ensuing days the basal level is higher than on the first and it is likely that a further increase occurs when the various bodily functions get into full swing. At any rate the demands of appetite rise sharply from the second to the fifth days, and thereafter continue to increase, though not so rapidly, to the twelfth day, the last of the present series. The amounts of food substances retained for growth may also increase a little, though of this we have at present no clear indication. Calculated in the manner above indicated, the average retention appears to be 15 calories per kilogram of body weight, with a variation for 50 per cent. of the cases of between 10 and 20 calories. Digestive work and excretory waste increase proportionally with the total intake. The former may tentatively be estimated at 5 per cent. and the latter (as shown by Holt) at 10 per cent. of the total calories. Both digestive work and waste are presumably smaller (perhaps by 5 or 10 calories) on maternal than on artificial feeding. The following scheme is provisionally suggested for the apportionment of the total intake, as given in Table 4, for the period from the fifth to the twelfth day:

Basal requirements (minimum heat production)....	45-55 calories
Retention for growth..............................	10-20 calories
Work of digestion.................................	4- 6 calories
General muscular activity.........................	20-30 calories
Waste	8-12 calories
Total (maximum caloric needs).............	87-123 calories

A word may be said as to the predictability of individual caloric needs. How closely can we estimate a given infant's total needs? Reference to Table 7 shows that after the fourth day, the probable error is about 15 per cent. of the mean values. This signifies that if we prescribe the mean or average quantity of the present series, we shall for one half of our cases be within 15 per cent. of the actual needs.

Since the probable error must be multiplied by four to cover all, or nearly all cases, it appears that the average requirement may at times fall 60 per cent. over or under the actual needs. Practically, the clinician, unless he is very conservative, will adjust his prescription for healthy infants to the point where the infant is usually satisfied. The mother who is herself regulating the baby's feeding will do likewise—she will nurse the baby until he stops crying.

SUMMARY

It appears probable that appetite provides a fairly accurate index to the needs of the new-born infant. In the series of eighty-five cases here reported, and with the formulas employed it also appeared to be a safe guide in so far as the avoidance of dangers to digestion is concerned. The demands of the infant for food exceed the basal requirements on the second day, equal the average total requirements of Benedict and Talbot on the third day; rise on the fifth day to the Heubner optimum of 100 calories, and thereafter rise slowly to about 115 calories near the end of the second week. That these demands are not excessive is indicated by the weight curve which, avoiding a greater initial loss than can be accounted for by mechanical factors, shows the same rate of gain as was previously established for healthy infants in the same community.

A final warning should be given that the method of feeding herein described, adopted for a special purpose, is not advocated for general use with breast fed infants. It may well be that for the conservation and increase of mammary secretion a period of partial starvation during the first week or two is useful or even necessary.

For infants who cannot have breast milk the claim of appetite to be satisfied may with less hesitation be given a hearing.

Grateful acknowledgment is made to Miss Katherine Crellin, head nurse of the obstetrical wards of Lane Hospital, and her assistants for the painstaking care with which the many weighings and other measurements of the present study were carried out; to Miss Fannie Hadden for valuable help with the compilations, and to Dr. F. J. Cajori of the department of chemistry of Leland Stanford Junior University for the analysis of corn syrup.

DATA IN THREE THOUSAND SEVEN HUNDRED AND FORTY-TWO PIRQUET TESTS *

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From August, 1913, to January, 1919, the Pirquet test was applied in the Babies' Hospital in 3,742 cases. It is the custom at the hospital to apply the test as a routine procedure in cases of acute and chronic illness, feeding cases, malnutrition, etc. It is not, as a rule, applied to children admitted for surgical operation for harelip, cleft palate, adenoids, tonsils, hernia, pyloric stenosis, etc. During the period covered in this study 7,494 children were admitted to the hospital. The test was applied in 3,742 cases, or in 49.9 per cent. of those admitted. The test was positive in 573 cases, or 15.3 per cent. Crude tuberculin, commonly known as Koch's O. T., furnished by the New York Department of Health, was used undiluted in every instance. The test was applied on the arm or leg. Two light scratches were made approximately ¼ inch in length and 2 inches apart. Into one scratch the tuberculin was lightly rubbed with a toothpick having a flat end; the other scratch was used as a control. In doubtful cases the test was repeated. It was not usually considered negative until forty-eight hours after application.

For purpose of study and for comparison with findings of others we have tabulated our results according to age, showing per cent. of positive Pirquet reactions (Table 1).

Of the entire group of 3,742 children tested, 2,204 were males and 1,538 females, with approximately the same proportion of positive tests for each sex, the former having 15.42 per cent. positive and the latter 15.14 per cent. positive.

The relation between white and negro children was rather significant. Although the number of negro children was small, these results confirm the observations of others regarding the greater prevalence of tuberculosis in the negro race, even in infancy and early childhood. In negro children 220 tests were made. Of these 45, or 20.45 per cent., were positive. Comparing these tests with 3,522 tests made in white children of whom only 528, or 14.99 per cent., were positive, it shows the incidence of tuberculosis among the negro race to be 5.5 per cent. higher than in the white race.

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* Received for publication April 3, 1922.

As our negro patients are drawn mainly from a section of the city in which the more prosperous negroes live, it is our impression that these figures are possibly lower than the average for the whole negro population of the city.

It must be remembered that these figures in no sense bear any relation to the incidence of tuberculosis in the community generally, but only to its frequency in the particular group which furnishes hospital patients. The patients on whom these studies have been made were reared in crowded city tenements, in boarding-out homes, and under other unfavorable environments unsuited to proper growth and development. Nor in our opinion do the hospital patients of medical wards caring only for infants and very young children represent an average of the tuberculosis incidence prevailing even in what may be termed the poorer classes.

TABLE 1.—RESULTS OF PIRQUET TEST ACCORDING TO AGE

Age	No. Tests	No. Positive Reactions	Per Cent. Positive
0-3 months	687	13	1.89
3-6 months	507	40	7.89
6-9 months	463	47	10.15
9-12 months	343	47	13.70
Under 12 months	2,000	147	7.35
12-18 months	487	83	17.04
18-24 months	363	68	18.73
12-24 months	850	151	17.76
2-3 years	371	107	28.84
3 years and over	521	168	32.24

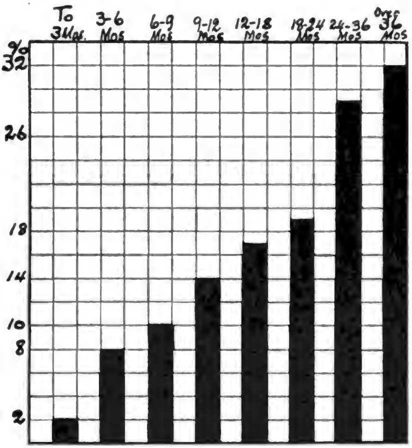
TABLE 2.—CLINICAL DATA ON FIVE HUNDRED AND SEVENTY-THREE CASES

Age	Died in Hospital	Unimproved	Improved	Cured	Total
0-3 months	7 (53.8%)	2	1	3	13
3-6 months	22 (55.0%)	11	3	4	40
6-9 months	19 (40.4%)	10	7	11	47
9-12 months	27 (57.4%)	6	3	11	47
Total under 12 months	75 (51.0%)	20	14	29	147
12-18 months	29 (34.9%)	22	10	22	83
18-24 months	22 (32.3%)	15	5	26	68
Total 2-3 years	51 (33.7%)	37	15	48	151
24-36 months	25 (23.3%)	16	10	56	107
3 years and above	10 (5.95%)	14	12	132	168
2 years and above	35 (12.7%)	30	22	188	275
Total	161 (28.0%)	96	51	265	573

The infant usually seen in the feeding wards of such a hospital is generally one who has had a prolonged history of disturbed nutrition associated with poor hygiene and neglect. Again, there are a large number of children with tuberculous meningitis or miliary tuberculosis who have been referred to the hospital as a last resort. In the hospital in which these studies were made there is an average admission of thirty cases of tuberculous meningitis a year. One is apt to receive the impression that tuberculous meningitis is a fairly common disease in infants; yet how infrequently are such cases, in fact any form of tuberculous infection in children, observed in private practice.

Table 2 gives the available data concerning the fate of the positive cases.

Of especial interest are 147 children under 1 year of age who gave a positive reaction. Seventy-five died in the hospital; seventeen others were removed, of whom seven had tuberculous meningitis and should be counted as fatal cases, thus making 54.6 per cent. of proven cases of tuberculosis, while ten had clinical evidence of probable tuberculosis in some other form on discharge. Twelve other children were discharged "unimproved," but without definite evidence of tuberculosis. Fourteen children were discharged "improved"; only one of these had clinical tuberculosis, while twenty-nine, or 19.3 per cent., were discharged as "cured" of the clinical condition for which they were admitted, having at no time while under observation shown any evidence of tuberculosis.



Increasing prevalence of tuberculosis with advancing age, showing per cent. positive in 3,742 cases.

Table 3 shows the clinical evidence of tuberculosis in the ten cases removed from the hospital.

The remaining seven cases were cases of tuberculous meningitis, tubercle bacilli having been found in the spinal fluid in every instance.

Cases Between Ages of 1 and 2 Years.—Of 151 children between 1 and 2 years of age who gave a positive reaction, fifty-one died in the hospital, forty-eight were cured of the condition for which they were admitted, fifteen were improved, and thirty-seven were removed against advice. Of these, twenty-nine had positive evidence of tuberculosis, six should be counted as fatal cases, as they had tuberculous meningitis when removed. This makes a total mortality of 37.7 per cent.

TABLE 3.—Data on Ten Cases Removed from Hospital

No.	Age. Mos.	Diagnosis	Family History and Exposure	Nursed
1	4½	Cervical adenitis	Negative	To present
2	4	Chronic tuberculosis of choroid	Ritual circumcision 8th day	To present
3	5	Acute miliary tuberculosis	Negative	To present
4	11	Pulmonary tuberculosis	Negative	3 months
5	11	Pulmonary tuberculosis	Negative	2 weeks
6	6	Tuberculous peritonitis	Negative	
7	8	Pulmonary tuberculosis	Father probably tuberculous	
8	8	Pulmonary tuberculosis	Negative	5 months
9	11	General miliary tuberculosis	Negative	2 months
10	9	Tuberculous meningitis, pulmonary tuberculosis	Negative	5 months

TABLE 4.—Clinical Data on Nonmeningitic Cases of Tuberculosis

No.	Age. Mos.	Diagnosis	Family History	Nursed
11	17	Tuberculous peritonitis	Negative	4 months
12	24	Tuberculous cervical adenitis	Negative	
13	13	Pulmonary tuberculosis	Negative	9 months
14	19	Pulmonary tuberculosis	Negative	9 months
15	21	Pulmonary tuberculosis	Negative	20 months
16	19	Pulmonary tuberculosis	Negative	3 months
17	15	Tuberculous adenitis		
18	17	Pulmonary tuberculosis, tuberculosis of knee	Negative	Nursed to present plus artificial food at 2 mos.
19	13	Tuberculous dactylitis	Negative	11 months
20	22	Tuberculous peritonitis	Negative	5 months
21	14	Pulmonary tuberculosis	Father had tuberculous laryngitis	1 years
22	19	Pulmonary tuberculosis	Negative	10 months
23	18	Subcutaneous tuberculous abscess	Mother died of "consumption" 8 mos. ago	Never nursed
24	17	Pulmonary tuberculosis	Negative	8 months
25	11	Pulmonary tuberculosis	Negative	3 months
26	14	Tuberculous peritonitis	Negative	5 months
27	20	Pott's disease	Negative	16 months
28	17	Pulmonary tuberculosis	Negative	3 months
29	22	Pulmonary tuberculosis, tuberculous peritonitis	Mother had pulmonary tuberculosis	1 month
30	15	Tuberculous hip, tuberculous abscess	Negative	3 months
31	24	General miliary tuberculosis, pulmonary tuberculosis	Negative	1 year
32	18	General miliary tuberculosis	Negative	6 months
33	18	General miliary tuberculosis	Negative	17 months

The clinical evidence of tuberculosis in the remaining twenty-three cases which were not meningitis is shown in Table 4.

Three of the infants discharged as "improved" had clinical evidence of tuberculosis.

One infant discharged as "cured" was in the hospital 292 days with tuberculous peritonitis.

Cases Between Ages of 2 and 3 Years.—Of 107 children between 2 and 3 years of age who gave a positive reaction, twenty-five died in the hospital, sixteen were removed, ten were discharged improved and fifty-six were cured. Of the sixteen removed, three had tuberculous meningitis and should be classed among the fatal cases, and ten had clinical evidence of tuberculosis in some other form. The total mortality, which includes the tuberculous meningitis cases, was 26.1 per cent.

Of the ten infants discharged as "improved," four had clinical evidence of tuberculosis. Of fifty-six infants discharged as "cured," two had clinical evidence of tuberculosis.

Cases at 3 Years of Age and Above.—Of 168 children three years of age and above, ten died in the hospital. Of fourteen removed against advice, eight had clinical evidence of tuberculosis of some variety. Of twelve discharged as "improved," three had evidence of tuberculosis in some form. Of the 132 discharged as "cured," none had any demonstrable signs of tuberculosis. The total mortality was 5.9 per cent.

It is a matter of importance to rule out any question of error in technic in such an analysis of cases. All the Pirquet tests in this study were made either by the resident physician of the hospital or one of the interns. These men are, in most instances, well trained and qualified to make such tests. There is always the personal equation in recording the results of the tests, which will have to be considered in any study embracing a large number of cases.

Regarding the question of the age of the tuberculin bearing on the reaction, Dr. William H. Park asserts that crude tuberculin should keep indefinitely, even at room temperature. It is possible in a large number of cases that occasionally the scarification was made either too deeply or not deeply enough, and, therefore, faulty technic might have influenced the reaction. Such an error would be discounted if the test were repeated once or successively. For this reason a second grouping is made of such cases as gave one or more negative reactions in which tuberculosis was definitely proven. There were fourteen such cases, with an average of 2.7 tests per case. As an index of the condition of the forty-four children at the time the tests were made, it should be noted that in twenty-eight instances the tests were made from one to five days before the death of the patient, and in five cases the test was done from five to eight days before death.

The fact that tuberculous infants in a very feeble condition frequently have a negative Pirquet test has been noted by many clinicians.

The poor condition of thirty-three of the patients in this group, judging their condition by the number of days intervening between their admission and death, probably explains the negative tests. However, nine infants had sufficient resistance to live ten days or more, and in these we should expect the test to be positive. Of these nine infants four had miliary tuberculosis, and in two the test had been repeated. Four were cases of tuberculous meningitis. The test had been repeated in three, and in one case it had been repeated six times. One of the nine infants had marasmus, and although it lived thirty days, it is

TABLE 5.—Negative Pirquet Reactions in Forty-Four Cases of Tuberculosis, Proved by Necropsy or the Finding of Tubercle Bacilli in the Sputum or Spinal Fluid

No.	Age, Mos.	Diagnosis	Days in Hospital	No. Tests	Positive Findings of Tuberculosis at Necropsy in Spinal Fluid and Sputum
34	15	Miliary tuberculosis	4	1	Necropsy
35	6	Miliary tuberculosis	5	1	Bacilli in sputum
36	42	Miliary tuberculosis	15	1	Necropsy
37	7	Miliary tuberculosis	1	1	Necropsy
38	14	Miliary tuberculosis	6	1	Necropsy
39	19	Miliary tuberculosis	3	2	Necropsy
40	9	Tuberculous meningitis	3	2	Necropsy
41	9	Miliary tuberculosis	9	3	Necropsy
42	22	Tuberculous meningitis, Pott's disease	10	2	Bacilli in spinal fluid
43	9	Miliary tuberculosis	3	2	Necropsy
44	8	Miliary tuberculosis	7	1	Necropsy
45	15	Tuberculous meningitis	7	3	Necropsy
46	12	Tuberculous meningitis	5	4	Bacilli in spinal fluid
47	11	Miliary tuberculosis	3	1	Necropsy
48	19	Tuberculous meningitis	5	2	Necropsy
49	1½	Tuberculous enteritis, miliary tuberculosis	2	1	Necropsy
50	30	Miliary tuberculosis, tuberculous peritonitis	42	2	Necropsy
51	43	Tuberculous meningitis	3	1	Bacilli in spinal fluid
52	11	Miliary tuberculosis, pulmonary tuberculosis	34	1	Bacilli in sputum
53	8	Miliary tuberculosis	24	2	Necropsy
54	9	Tuberculous meningitis	1	1	Bacilli in spinal fluid
55	29	Tuberculous meningitis	12	7	Bacilli in spinal fluid
56	14	Tuberculous meningitis	1	1	Necropsy
57	40	Tuberculous meningitis	3	2	Necropsy
58	11	Miliary tuberculosis	5	1	Necropsy
59	13	Tuberculous meningitis	3	1	Necropsy
60	7	Miliary tuberculosis	5	1	Necropsy
61	3	Miliary tuberculosis	4	1	Necropsy
62	10	Miliary tuberculosis	3	1	Necropsy
63	3½	Tuberculous meningitis	3	1	Necropsy
64	19	Tuberculous meningitis	10	1	Necropsy
65	42	Tuberculous meningitis	16	3	Necropsy
66	2	Marasmus	30	1	Necropsy
67	20	Empyema-pericarditis	2	1	Necropsy
68	11	Tuberculous meningitis	3	2	Necropsy
69	18	Tuberculous meningitis	2	1	Necropsy
70	36	Acute purulent pericarditis	8	1	Necropsy
71	5	Miliary tuberculosis	1	1	Necropsy
72	8	Tuberculous meningitis	6	1	Necropsy
73	4½	Regulation of feeding	3	1	Necropsy
74	30	Tuberculous meningitis	4	1	Necropsy
75	16	Tuberculous meningitis	5	1	Necropsy
76	13	Tuberculous meningitis	3	1	Necropsy
77	18	von Jaksch's anemia	..	1	Necropsy

probable that the poor nutrition of the infant was the cause of the negative reaction.

The following cases included in Table 5 seem of sufficient interest to merit further comment:

SYNOPSIS OF CASES

Cases 1 and 2 (Nos. 46 and 65).—Japanese, ages 12 months and 3½ years, respectively; tuberculous meningitis. The first child was admitted in poor condition and had four negative tests while under observation. The second child was admitted in good condition and had three negative tests while under observation.

Case 3 (No. 60).—Age, 7 months. Discharged from the hospital eight days previously with a diagnosis of ileocolitis, "cured." At the same time the Pirquet test was positive. When readmitted, the child's condition was poor and the Pirquet test was negative. The father was in the hospital under treatment for pulmonary tuberculosis.

Case 4 (No. 49).—Age, 6 weeks, breast feeding exclusively, abdomen distended since birth, no known exposure to tuberculosis.

Of this group of forty-four cases with negative Pirquet tests and positive evidences of tuberculosis, seven infants had been entirely breast fed from birth.

Of the entire group of forty-four cases of proven tuberculosis with negative Pirquet tests, twenty infants had tuberculous meningitis; nineteen others had miliary tuberculosis (seventeen proved by necropsy and two by finding tubercle bacilli in the sputum). The other five infants had other forms of tuberculous infection demonstrated at necropsy. Of those with tubeculous meningitis, fifteen had poor or very poor nutrition, four had fair, and only one had good nutrition. Of those with miliary tuberculosis, twelve had poor or very poor nutrition and seven had fair nutrition.

The youngest of these infants was 6½ weeks old, and the oldest 43 months. Twenty-two of the children were under 12 months.

0- 3 months	4 cases
3- 6 months	3 cases
6- 9 months	9 cases
9-12 months	6 cases
12-18 months	8 cases
18-24 months	5 cases
24-36 months	4 cases
36 months and over	4 cases

Positive Reactions in Breast-Fed Infants Without History of Exposure.—Thirty-one cases have been assembled with the view of presenting the difficulty of determining the mode of infection of many of the cases of tuberculosis in infancy and childhood.

It has often been stated that the most dangerous types of persons with pulmonary tuberculosis are those who do not known they have the disease and those who think they have been cured. In obtaining a history of exposure, the first type cannot be excluded, except by the most rigid social service cooperation, which has not been at any time available to us. In so far as the so-called "cured" cases are concerned, we believe that a careful history generally elicits the information that some one in the family has had pulmonary tuberculosis at some time. In twenty-nine of the thirty-one cases, the children had been nursed entirely up to the time of admission to the hospital, or within a few days to a week prior to admission. In two of the cases the infants had been nursed twelve and fourteen months, respectively; the former was 14 months of age and the latter 18 months.

The fact that twenty-nine of the infants had been nursed entirely would seem to rule out the possibility of a bovine infection. Nineteen of the thirty-one infants had either tuberculous meningitis or miliary tuberculosis or both, one had tuberculous cervical adenitis, and one had pulmonary tuberculosis with tubercle bacilli in the sputum; none of the others had a demonstrable tuberculous lesion, yet all had a positive reaction. In view of the fact that every infant in this group of cases had been breast-fed, it seems probable that in every instance the infection was acquired from a human contact. In spite of this presumption, certainly in thirty of the thirty-one cases, the history offered no evidence that the parent or parents were aware of the fact that the child had been in contact with a tuberculous person. The average age for the thirty-one infants was 8 months.

TABLE 6.—Cases with Positive or Doubtful Reaction and Negative Necropsy Findings for Tuberculosis *

No.	Age, Mos.	Diagnosis	Family History and Exposure	Findings at Necropsy	Pirquet Test
78	13	Empyema..................	Negative	Bronchopneumonia; no tuberculosis	Positive
79	9	Acute bronchopneumonia.	Negative	Negative for tuberculosis	Doubtful, probably negative
80	17	Marasmus; tetany.........	Negative	Glioma of brain; negative for tuberculosis	Four slightly positive tests, negative after 24 hrs.
81	10	Glioma of cerebellum......	Negative	Tumor of cerebellum; negative for tuberculosis	Doubtful, counted negative
82	26	Cerebral tumor; chronic hydrocephalus	Negative	Glioma of brain; negative for tuberculosis	Slightly positive
83	15	Pneumococcus septicemia; tetany; empyema	Negative	Negative for tuberculosis	Slightly positive

* It is of interest, but probably of no significance, that in three of these cases a brain tumor was found at necropsy.

Positive Reactions in Very Young Infants.—The details relating to thirteen infants under 3 months of age with positive reactions are especially important because the mother had positive tuberculosis in four instances and there was a probable tuberculous exposure in three instances. In six cases there was no history of tuberculosis in the family and no exposure was known. Of the four cases in which the mother definitely had tuberculosis three of the infants had proven tuberculosis, and the fourth infant was discharged "cured" of the condition for which it was admitted. In the three cases with a probable exposure, one infant died and had tuberculous lesions at necropsy; the remaining two were discharged from the hospital; one was "improved" and the other "unimproved." Of the six infants without a history of exposure two died in the hospital. Positive findings were recorded at

TABLE 7.—Positive Reactions in Breast-Fed Infants Without Exposure

No.	Age, Mos.	Diagnosis	Family History and Exposure	Nursed
84	14	Tuberculous meningitis, miliary tuberculosis..	Negative	1 year, + solid food since
85	8	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
86	4½	Trachael stenosis due to tuberculous bronchial lymph nodes	Negative	Entirely
87	18	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
88	4	Acute cervical adenitis..........................	Negative	Entirely
89	7½	Miliary tuberculosis, tuberculous meningitis, tuberculous enteritis	Negative	Entirely
90	12	Tuberculous meningitis, miliary tuberculosis..	Negative	11½ months, artificial feeding since
91	4	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
92	11	Tuberculous meningitis.........................	Uncle who lived in same house 8 mos. had pulmonary tuberculosis	Entirely
93	11	Pulmonary tuberculosis........................	Negative	Entirely
94	5	Pulmonary tuberculosis, miliary tuberculosis..	Negative	Entirely
95	10	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
96	8	Pyelitis..	Negative	Entirely
97	5	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
98	8	Tuberculous meningitis........................	Negative	Entirely
99	9	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
100	5	Acute miliary tuberculosis......................	Negative	Entirely
101	5½	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
102	3	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
103	10	Tuberculous meningitis, miliary tuberculosis..	Negative	Entirely
104	14	Ileocolitis.......................................	Negative	Entirely
105	4	No disease......................................	....	Entirely
106	15	Tetany..	....	Entirely
107	12	Acute bronchopneumonia......................	Negative	Entirely
108	1½	Acute gastro-enteritis..........................	....	Entirely
109	5	Retropharyngeal abscess......................	....	Entirely
110	6	Tuberculous meningitis.........................	Negative	Entirely
111	7	Secondary anemia..............................	....	Entirely
112	6	Defective cerebral development................	....	Entirely
113	7	Tuberculous meningitis.........................	....	Entirely
114	9	Tuberculous meningitis.........................	....	Entirely

TABLE 8.—Data Regarding Nine Children 12 Months Old or Less When Pirquet Reaction Positive

No.	Age at Test, Mos.	Age at Present, Mos.	Race	Present Weight, Pounds	Information Obtained by Field Worker
128	11	30	Negro	..	Very healthy child, well nourished
129	6	34	American	..	Neighbor states that child is healthy
130	7	12	Italian	..	Mother states child is well; field worker noted child was pale
131	12	55	German	38	Mother states he is healthy
132	10	48	American	..	Healthy
133	2	18	Italian	20	Coughs, underweight
134	12	54	Italian	35	Underweight, no symptoms
135	8	48	Hungarian	39	Healthy
136	3	32	Irish	27½	Healthy

necropsy. Another infant died of meningococcus meningitis. Necropsy was not obtainable. Three infants were discharged "cured."

Of the thirteen cases, there was no other evidence of tuberculosis than the skin test in six, while the patients were under observation. Six patients died of tuberculosis in the hospital. It was possible to obtain data regarding only one of the six patients discharged from the hospital. At the time this information was secured the child (No. 127) was 14 months old, weighed 11 pounds 11 ounces, and was under treatment for "spastic paralysis."

SUMMARY OF CASES

Case 5 (115).—White, aged 2 months; in hospital thirty-eight days. Nursed two weeks. Mother is in hospital with laryngeal tuberculosis. Necropsy: General miliary tuberculosis and tuberculous meningitis.

Case 6 (116).—White, aged 3 months; in hospital six days. Artificially fed. Mother has active pulmonary tuberculosis; cared for infant. Tuberculous skin lesions. Tubercle bacilli found in sputum.

Case 7 (117).—White, aged 3 months; in hospital eight days. Artificially fed. Mother living at home had pulmonary tuberculosis. Tuberculous meningitis.

Case 8 (118).—Negro, aged 3½ months; no exposure; nursed one month.

Case 9 (119).—White, aged 2½ months. Maternal grandmother has pulmonary tuberculosis. Nursed one month.

Case 10 (120).—White, aged 2 months; in hospital twenty days. Mother thought to have pulmonary tuberculosis. Nursed one day.

Case 11 (121).—White, aged 9 weeks; in hospital thirty days. Mother in hospital with pulmonary tuberculosis. Artificially fed.

Case 12 (122).—White, aged 3 months. Died after three days' observation. Family history and exposure negative. Nursed three weeks. Tubercle bacilli found in sputum. Tuberculous lesions found at necropsy.

Case 13 (123).—White, aged 3 months. Diagnosis: Tuberculous meningitis. Family history and exposure negative. Nursed entirely. Tuberculous lesions found at necropsy.

Case 14 (124).—White, aged 6 weeks; in hospital four days. Discharged "cured." No family history or exposure. Nursed entirely.

Case 15 (125).—White, aged 2½ months. Diagnosis: Meningococcus meningitis. Died. No necropsy. No family history or exposure. Two Pirquet tests, both slightly positive.

Case 16 (126).—White, aged 2 months. Diagnosis: Tuberculous meningitis. Tuberculous lesions found at necropsy. Mother probably tuberculous. Nursed three days.

Case 17 (127).—White, aged 3 months. Family history and exposure negative. Nursed one month. Now 14 months old. Weight 11 pounds 11 ounces. Diagnosis: "Spastic paralysis."

Relation to Exposure.—In a group of 433 cases, which includes children with positive and negative Pirquet tests with positive findings of tuberculosis as necropsy in spinal fluid or sputum, there was a relation to exposure in a considerable number of the cases.

Exposure definite in 77 cases, or 17.7 per cent.
Exposure very probable in 10 cases, or 2.3 per cent.
Exposure probable in 21 cases or 4.7 per cent.
No history of exposure in 325 cases, or 75 per cent.

THE VITAL CAPACITY OF THE LUNGS OF CHILDREN

A PRELIMINARY REPORT *

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It is now definitely recognized that disease of the lungs or of the heart may produce a considerable reduction in the vital capacity of the lungs. Due to the fact that the normal lung capacity, particularly for children, is not generally known, clinicians have experienced difficulty in estimating accurately the extent of the reduction in vital capacity existing in individual cases. As a result such determinations are rarely included in the routine examination of children suffering from alleged cardiac or pulmonary disease.

Rather extensive series of observations made on healthy children have been published especially by Gilbert,[1] Smedley,[2] Baldwin,[3] Emerson and Green[4] and Wilson and Edwards.[5] Unfortunately, most of these data have appeared in journals not readily accessible to the medical profession. We wish to contribute vital capacity averages for 430 healthy children (228 boys, 202 girls), ranging in age from 4 to 15 years inclusive. In addition, observations are reported for five children having bronchiectasis, and for five with tuberculosis.

The vital capacities were measured by means of an accurately calibrated wet spirometer. The children were instructed to take the deepest possible inspiration, and then to empty the lungs completely into the spirometer. Each child was given several trials, and the maximum amount repeatedly expired was recorded as the vital capacity.

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[1] Gilbert, J. A.: Researches on the Mental and Physical Development of School Children; Studies from Yale Psychological Laboratory, 1894, **2**: p. 40. Researches on School Children and College Students, University of Iowa Studies in Psychology, 1897, **1**: p. 1.

[2] Smedley, F. W.: Report of Commissioner of Education, **1**:1095, 1902.

[3] Baldwin, B. T.: Physical Growth and School Progress, U. S. Bureau of Education Bull. No. 10, 1914, p. 6.

[4] Emerson, P. W., and Green, H.: Vital Capacity of the Lungs of Children, Am. J. Dis. Child. **22**:202 (Aug.) 1921.

[5] Wilson, M. G., and Edwards, D. J.: Vital Capacity of the Lungs and Its Relation to Exercise Tolerance in Children with Heart Disease. Standards for Normal Vital Capacity for Children. The Lung Capacity in Certain Intrathoracic Conditions, Am. J. Dis. Child. **22**:443 (Nov.) 1921.

When the cooperation of the child was unsatisfactory the observations were discarded. Care also was taken to include no child suffering either from acute respiratory infections, or from chronic heart or lung disease.

The children were weighed naked, and at the same time the standing height was recorded. The sitting height was measured with the child seated on a chair against a perpendicular scale.

The vital capacity of the lungs for the boys (Table 1) shows an increase with advancing age, from an average of 792 c.c. at 4 years to 3,044 c.c. at 15 years, a gain of 2,252 c.c. For the girls, during a similar period the averages increase from 644 c.c. to 2,381 c.c. Thus for the latter the growth in lung capacity amounting to 1,737 c.c. is considerably less than that accomplished by the former (2,252 c.c.). The data also show the vital capacity to be constantly lower for girls than for boys at corresponding ages.

TABLE 1.—AGE, NUMBER OF NORMAL BOYS AND GIRLS, AVERAGE VITAL CAPACITY (SEXES SEPARATED)

Age, Years	Number of Boys	Vital Capacity Boys, C.c.	Vital Capacity Girls, C.c.	Number of Girls
4	6	792	644	9
5	15	936	819	12
6	19	1,161	1,055	26
7	27	1,320	1,214	18
8	32	1,480	1,337	17
9	37	1,740	1,511	19
10	14	1,828	1,740	23
11	24	1,954	1,782	19
12	16	2,309	2,061	19
13	18	2,383	2,268	24
14	15	2,653	2,525	8
15	5	3,044	2,681	8

TABLE 2.—WEIGHT, NUMBER OF NORMAL BOYS AND GIRLS AND VITAL CAPACITY (SEXES SEPARATED)

Weight, Kg.	Number of Boys	Vital Capacity Boys, C.c.	Vital Capacity Girls, C.c.	Number of Girls
10-15	3	978	693	7
20	45	1,071	975	50
25	66	1,438	1,366	59
30	38	1,783	1,675	34
35	29	2,058	1,911	33
40	24	2,323	2,061	13
45	11	2,509	2,377	11
50	6	2,800	2,533	6
55	5	3,108	2,713	4

In Tables 2, 3 and 4 the data are averaged (sexes separated) according to body weight (in kg.), standing height (in cm.) and sitting height (in cm.), respectively. At this time we will call attention merely to the fact that at either corresponding weight, standing height, or sitting height, the average vital capacity is constantly greater for the boys than for the girls. The actual averages for the different body measurements recorded may be obtained by reference to the proper table.

In addition to presenting data for normal children, we are also able to report vital capacity records for five children having bronchiectasis (Table 5). These children were examined by one of us, while working at the Mayo Clinic. The diagnosis in each instance was confirmed by roentgen-ray examination of the lungs. The children gave histories of repeated attacks of bronchitis extending over a long period, and at the time seen complained of frequent colds, chronic cough, abundant sputum and were in general poor health. With Subjects 1 and 2 (Table 5) definite clubbing of the terminal phalanges of the fingers and toes was noted. Physical examination in each instance revealed the presence of numerous coarse râles particularly at the bases of the lungs.

TABLE 3.—STANDING HEIGHT, NUMBER OF NORMAL BOYS AND GIRLS AND AVERAGE VITAL CAPACITY (SEXES SEPARATED)

Standing Height, Cm.	Number of Boys	Vital Capacity Boys, C.c.	Vital Capacity Girls, C.c.	Number of Girls
95-100	5	732	625	5
105	7	850	742	9
110	12	967	902	17
115	19	1,163	1,082	21
120	25	1,323	1,182	10
125	27	1,442	1,302	20
130	33	1,688	1,495	16
135	24	1,790	1,730	14
140	20	1,964	1,835	23
145	15	2,227	1,926	25
150	8	2,418	2,175	10
155	16	2,510	2,348	11
160	13	2,842	2,527	15
165	7	3,210	2,812	3

TABLE 4.—SITTING HEIGHT, NUMBER OF NORMAL BOYS AND GIRLS AND VITAL CAPACITY (SEXES SEPARATED)

Sitting Height, Cm.	Number of Boys	Vital Capacity Boys, C.c.	Vital Capacity Girls, C.c.	Number of Girls
55-57.5	13	855	812	13
60.0	18	1,074	1,020	26
62.5	23	1,250	1,149	17
65.0	39	1,408	1,367	28
67.5	37	1,624	1,589	21
70.0	37	1,909	1,623	28
72.5	19	2,127	1,881	21
75.0	17	2,347	2,075	14
77.5	15	2,583	2,406	17
80.0	7	2,900	2,557	7

The data (Table 5) show the existence of a considerable reduction in vital capacity for the first four patients, which is especially pronounced (46 per cent.) for Subject 2. Subject 4 was examined on a second occasion, and her vital capacity again registered 750 c.c.

This time she was instructed to endeavor to free the bronchi of accumulated secretion by postural cough with the head hanging downward and at a lower level than that of the chest. After expectorating a considerable amount of sputum in this manner, the vital capacity was again recorded, and was found to have increased from 750 to 1,150 c.c. For Subject 5 the vital capacity actually exceeded the normal average, expected for corresponding age. This girl, however, had been freeing the lungs of excessive secretion by means of postural cough for several weeks, which possibly was a factor in enabling her to register a vital capacity equal to the normal.

Although five cases is too small a number to justify any sweeping statements, nevertheless, it appears safe to conclude that bronchiectasis usually produces a definite reduction in the vital capacity of the lungs, which may be very marked in severe cases. In certain instances, however, the vital capacity may be practically normal in spite of the presence of definite chronic disease of the lungs. A normal vital capacity consequently does not necessarily indicate that the lungs are in a perfectly normal condition.

TABLE 5.—Age in Years, Standing Height in Cm., Weight in Kg., Vital Capacity in C.c., and Normal Vital Capacity for Corresponding Age for Five Children Having Bronchiectasis

Case Number	Age, Years	Standing Height, Cm.	Weight, Kg.	Vital Capacity, C.c.	Normal Vital Capacity for Corresponding Age, C.c.
Boys:					
1	8	127	21.4	1,000	1,480
2	15	168	41.0	1,375	3,044
Girls:					
3	6	120	24.1	800	1,055
4	7	121	18.0	750	1,214
5	12	147	30.5	2,200	2,061

The vital capacity measurements for five children having tuberculosis are recorded in Table 6. For the two boys the vital capacity of the lungs is extremely subnormal. The first boy has an advanced and active tuberculosis of the lumbar spine complicated by a large psoas abscess. The roentgenograms of the lungs revealed diffuse mottling and fibrosis throughout both lung fields. About six months later a second determination was made, and the vital capacity showed a decrease from 1,050 to 775 c.c. The hospital records revealed that this boy had failed gradually in strength during this period, and was in a much poorer general condition than when first examined.

The second boy's vital capacity is also greatly reduced. He has a healed Pott's disease of the thoracic vertebrae, with extensive ankylosis and a marked kyphosis. Numerous scars of healed sinuses are present along the spine. The roentgen-ray revealed a chronic fibroid condition in the lungs. In spite of the enormous reduction in vital capacity, this boy was able to undergo considerable activity with comparatively little dyspnea.

The vital capacity for the first one of the three girls reported is practically normal for her age. She had an active tuberculosis of the hip with many discharging sinuses. The roentgen-ray revealed normal lung fields, and only moderate enlargement and calcification of the glands at the root of the lungs.

The second girl has an advanced and active pulmonary tuberculosis with many areas of consolidation in each lung. Numerous râles are present on both sides, and examination of the sputum revealed many tubercle bacilli. As might be expected, the vital capacity of the lungs of this patient was greatly reduced.

TABLE 6.—~~Age, Standing Height, Weight, Vital Capacity,~~ Normal Vital Capacity for Corresponding Age, ~~Location and~~ Extent of ~~Disease~~ for Five Children Having Tuberculosis

Case Number	Age, Years	Standing Height, Cm.	Weight, Kg.	Vital Capacity, C.c.	Normal Vital Capacity for Corresponding Age C.c.	Location and Extent of Tuberculosis
Boys:						
1	13	142	21.8	1,050	2,383	Lumbar spine; psoas abscess
2	15	131	23.2	750	3,044	Thoracic spine; marked hyphosis; chronic fibroid; pulmonary tuberculosis
Girls:						
3	11	138	29.0	1,600	1,782	Hip; many sinuses; lungs negative
4	15	151	50.1	950	2,681	Advanced pulmonary tuberculosis
5	13	146	25.1	575	2,288	Advanced pulmonary with cavities

The third girl has an advanced pulmonary tuberculosis with cavities present in each lung. At the time the record was made the girl was up and about, and practically free from dyspnea on mild exertion, in spite of the fact that her vital capacity was only slightly more than one third the normal expected for corresponding age. The observation recorded was obtained about three months previous to the death of the patient.

These cases illustrate the extreme reduction in the vital capacity of the lungs which may result from pulmonary tuberculosis. Undoubtedly, these patients at one time had a normal vital capacity, but following the development of a tuberculous infection, the vital capacity apparently progressively decreased as the pathologic process advanced. Repeated determinations made during this period probably would have given striking and unmistakable evidence through the progressive diminution in vital capacity, that the pathologic condition present in the lungs was gradually increasing. While single measurements of the vital capacity are no doubt of value in detecting the presence of pulmonary diseases, repeated determinations are vastly more valuable, for changes in the pathologic process present are promptly reflected by fluctuations in the vital capacity of the lungs. Therefore, the progress of the disease may be followed by noting the effect on the vital capacity. Instead of relying on indefinite clinical notes or memory regarding the presence of abnormal breath sounds, or extent of areas of dulness, etc., recorded on previous examinations, an accurate measurement in cubic centimeters of the vital capacity of the lungs can be established from which except for the normal increase accompanying growth there should be very little constant deviation on subsequent examinations. The occurrence of any permanent reduction in the vital capacity below previous determinations apparently will give immediate clue to the development or extension of pathologic processes within the chest.

SUMMARY

1. The averages for the vital capacity of the lungs of 430 healthy children (228 boys; 202 girls), grouped according to age, weight, standing height and sitting height, are recorded. The averages show the vital capacity of the lungs to be constantly greater for the boys than for the girls of corresponding age and size.

2. Vital capacity records are reported for five children having bronchiectosis and also for five children suffering from tuberculosis, which demonstrate the marked reduction in vital capacity which these conditions may produce.

NEUROPATHIC MANIFESTATIONS IN INFANTS AND CHILDREN AS A RESULT OF ANAPHYLACTIC REACTION TO FOODS CONTAINED IN THEIR DIETARY *

W. RAY SHANNON, M.D.

ST. PAUL

The close association of the exudative and neuropathic diatheses suggests a causal relationship. The frequent anaphylactic nature of the former [1] would seem to point toward a similar cause in the latter. It is my purpose in this paper to discuss certain nervous manifestations in infants and children from the standpoint of anaphylactic cause.

It is hardly necessary to call attention to the frequent occurrence of the exudative and neuropathic diatheses in the same individual. All observers recognize the common association. However, it seems to have been generally held that this relationship is nothing more than accidental. Czerny considered it so.[2] He felt that the almost universal presence of the neuropathic diathesis in one or both parents of children with the exudative diathesis led, as a natural result, to the neurotic child. The degree to which the infant was affected by this nervous environment determined, to a certain extent, the obstinacy and severity of the exudative manifestations. Pfaundler [3] stated that the sneezing in coryza, pertussoid in bronchitis, asthma in bronchiolitis, severe colic in enteritis, etc., were dependent, to a certain degree, on the coexistence of a neuropathic diathesis along with the exudative diathesis.

This common association, together with the fact that frequently in the same individual the symptoms of one, and again the symptoms of the other diathesis, will seem to predominate, led me to the opinion that not infrequently the symptoms of both conditions might be due to the same underlying factor. Inquiry revealed the fact that often nervous patients have a history, either personal or familial, of exudative disturbances, and the frequent anaphylactic basis for the exudative phenomena suggested that the nervous symptoms might also be due to this cause. Therefore, this investigation was undertaken to see if this might not be the case clinically.

The cases presented are of three types; first, the type in which the symptoms of both diatheses were plainly present; second, the type in

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* Received for publication March 28, 1922.

* From the Miller Hospital Clinic.

1. Shannon: Minnesota Med. **5**:137. (March) 1922.
2. Czerny: Monatschr. f. Kinderh. **7**:1. 1908.
3. Pfaundler: (Quoted from Leo Wolf). Jahrb. f. Kinderh., **4**:175.

which the present symptoms were nervous but in which there was a definite exudative history; and third, the type in which the symptoms were those of the neuropathic diathesis without a history of frank exudative phenomena preceding. With one case experimentation was possible.

REPORT OF CASES

Case 1. A girl, 5 years of age, presented an uriticarial eruption and asthma. The mother stated that the patient was very high-strung and nervous. There was a history of hay-fever in the father and of eczema in several cousins. Skin tests revealed positive erythematous reactions to several foods of which the patient was eating a great deal. Removal of the offending foods from the patient's diet resulted in early relief from nervous manifestations and from the uriticaria and asthma.

Case 2. A boy, 2 years and 8 months of age, had a history of a very itchy skin eruption, apparently of an urticarial nature, rather loose stools, and extreme nervousness. Whereas he normally slept well at night and took a nap during the daytime, of late he would not sleep at all during the day and very poorly at night. He was very irritable.

Cutaneous tests showed erythematous reactions to a number of foods he was eating. Modification of the diet and eliminating as much as possible the foods to which he was sensitive resulted in complete disappearance of the skin and nervous symptoms in two weeks' time. The child became himself again, was not irritable, slept well at night, and took a long nap during the daytime.

Case 3. A boy, 4 years old, had a history of eczema and asthma. He was extremely high-strung and very nervous. His appetite was rather poor and he was very finicky about what he ate. He slept poorly at night. The mother complained that he could not sit still and that he was very hard to manage. Skin tests revealed erythematous reactions to a large number of foods and to a number of animal emanations. The diet was regulated and he was instructed to stay away from the animals to whose proteins he was sensitive. Relief from asthmatic symptoms had occurred nine days later and the eczema had improved considerably. Eighteen days after the tests were performed he was still free from asthma and there was only a slight chapping of the cheeks. The nervousness had improved greatly. His general restlessness was gone. He slept better at night and slept well during the daytime. His appetite was very good and he had gained 2½ pounds in weight. At the present time, one month after the institution of treatment, the improvement has continued.

Case 4. A girl, 28 months old, was brought in because of an urticarial eruption and nervousness. Local treatment for the urticaria only was advised. Three weeks later she was brought back. The skin condition seemed improved, but the mother stated that the child was very irritable. She was unruly, peevish, ate poorly, and did not sleep well.

Skin tests revealed positive reactions to a number of foods the patient was eating in rather large quantity. These included egg and wheat. A diet was advised eliminating, as nearly as possible, the offending foods. Improvement was noted one week later but the mother said that she had been giving store cookies containing both egg and wheat to the patient. These were discontinued and after another interval of two weeks there was considerable improvement, especially in the nervousness. The mother asserted that the child "could be reasoned with." On one occasion the patient had been given spaghetti and tomatoes for her evening meal and both skin and nervous symptoms were much worse thereafter. At the present time, six weeks after the tests were performed, the nervousness is gone and the skin is clear.

Case 5. A boy, 12 years of age, had been subject to eczema when an infant, to hives as he grew older, and still later to attacks of asthma. All these symptoms had been absent for a number of years, with the exception that he had

had an attack of urticaria a few months previous to the first observation. The present complaint was that of fever for the past few days, extreme nervousness, constant stuffiness in the nose, occasional attacks of vomiting, and frequent headaches. He was extremely introspective, cried easily, was very irritable, and was constantly "out of sorts."

A period of hospital study revealed a chronic inflammatory condition of the nasal sinuses. Treatment of this condition resulted in relief from the headaches and disappearance of the fever and nasal obstruction. However, the nervousness remained.

Skin tests revealed sensitization to several foods, a number of pollens, although the parents had never suspected the presence of hay-fever, and to horse dandruff and dog hair. A diet was advised and the patient instructed to stay away from dogs and horses.

Prompt improvement in the nervous symptoms resulted and this has been permanent over a period of seven months, except for a single attack of vomiting.

Case 6. A boy, 8 years old, was brought in because he was extremely irritable, did not eat well, was cruel to his playmates, and was unable to apply himself at school. As a result of the latter condition, he spent two years in the first grade.

He had been perfectly normal, except that he had had head colds almost from birth until he was 4 years old. At that time he had had a series of convulsions without ascribable cause. He was studied by nerve specialists, internists, and eye, ear, nose and throat men, the final impression of the physician in charge being that the convulsions were due to a "food poisoning" of some kind. There had been no convulsions since that time.

A complete physical examination, including blood, spinal fluid and urine studies, Wassermann test, Pirquet test, failed to reveal anything abnormal. There was no family history of sensitization phenomena. Cutaneous tests revealed positive erythematous reactions to wheat, spinach, egg white, whole egg, pear, orange, pea, beef and figs. Questionable reactions were obtained to lactalbumin and banana. The patient was instructed to eat no wheat cereal or pastries, spinach, egg white, pea, orange, pear, beef, figs, or banana. He was to eat rye bread.

Nothing was heard from him for six weeks, when the mother reported that the boy had been a different child from the time he had gone on the diet. His irritability was lessened; he was no longer cruel to his playmates; he was doing well in school, and his appetite was good. When heard from again three months after the diet was instituted the improvement had continued and he had made his grade in school without difficulty.

Case 7. A boy, 9 years of age, suffered from extreme nervousness and attacks of vomiting. The periodic attacks ordinarily came on infrequently, not oftener than once a month. Usually he would vomit but once but was always indisposed for several days thereafter. Between the attacks he was irritable, slept poorly, and was very finicky about what he ate. He was extremely highstrung. For the past two weeks he had been vomiting every third day, would eat almost nothing between attacks, and was so irritable that he was a problem to his parents.

His past history was negative for protein sensitization, with the possible exception that he had been a difficult feeding case from 3 to 14 months of age. From that time until four or five years he had been perfectly well. The vomiting attacks began at that time. He always coughed when he caught cold. When first seen he had been under treatment for some time for nasal sinusitis.

The immediate family history was negative for asthma, hay-fever, urticaria, or eczema. One sister had had similar vomiting attacks at one time in her life. One cousin could not eat eggs because they poisoned her. The paternal grandfather had had attacks of difficult breathing in his old age which apparently resembled asthmatic attacks.

Physical examination revealed nothing except that the patient was somewhat pale and undernourished. He was, therefore, tested with the foods of his dietary. Positive erythematous reactions were obtained to wheat leucosin, wheat gliadin, wheat proteose, pea, pineapple, potato and navy bean. The reactions to fig, brazil nut and rye were questionable.

The patient was instructed to eat no peas, navy beans, string beans, lima beans, pineapple, figs or brazil nuts. He was to eat potato no more than four times weekly, and no wheat cereal or pastries made from wheat flour. Rye bread only was to be eaten, with the exception of a small amount of white bread toast. Arrowroot or corn-starch were to be used for thickening gravies.

Improvement was almost immediate. There were no more vomiting spells. His appetite became ravenous. The mother said that she could not "fill him up." All signs of nervous irritability ceased very shortly after the diet was instituted. He began to sleep all night and to waken refreshed, which he did not do before. During the following month his class standing rose from thirteenth, where it had been constantly for five months past, to eighth, without any conscious effort on his part. At present, two and a half months after the diet was prescribed, there has been no return of either nervousness or vomiting.

Case 8. Girl, aged 5 months, suffered from undernutrition.

The family history was unfortunate. The child was illegitimate and nothing was known of the father. The mother was committed to an institution for the feebleminded after deserting the infant.

The baby was partially breast fed for two mouths and since that time had been fed on milk mixtures. Cream of wheat was added to the infant's diet and seven days thereafter it was noticed that the child was extremely restless. There was constant movement of the arms and legs, with jerky movements of the entire body. The infant constantly turned and twisted in her crib. She cried incessantly day and night and slept but little throughout the twenty-four hours.

No cause was found on physical examination. There was no evidence of infection; the skin was clear and the stools normal. The symptoms were attributed to a nervous diathesis, dependent on the questionable heritage, and bromids were prescribed. These afforded marked relief and were discontinued after a short time. The infant immediately reverted to her former condition. Again bromids were given and the condition was controlled for a considerable period. However, they gradually lost their effect and about three months later (January, 1922), the patient's condition was as bad as it had been before the bromids were started.

January 25 cutaneous tests were performed with several cereals, vegetables and cow's milk. Positive reactions were obtained to wheat leucosin, proteose and globulin. All of the rest were negative. Wheat cereal was discontinued and oatmeal substituted. The bromid was discontinued.

One week later the child's disposition had changed remarkably so that it was noticed by all who came in contact with her. She slept all night and was playful and happy during the daytime. She cried but little. She had gained 7½ ounces during a period of four days.

February 5 cream of wheat was again added instead of the oatmeal. Twelve hours later a return of the old irritability was noticeable. She was very restless all the next day, turning, twisting, and throwing herself about in her crib. That night she slept less well and cried a part of the night. The symptoms continued throughout the seventh and that night she cried all night. February 8 the cream of wheat was discontinued and oatmeal again substituted. Improvement was prompt and by the night of the thirteenth the patient slept all night. By February 17 she was happy and playful, as she was during the first experimental period. Since that time she has remained so.

Of the cases cited the first four presented skin eruptions. The natural explanation for the nervousness in these cases is that it is the reasonable accompaniment of the skin irritation. However, in all but Case 1 the nervous manifestations were out of all proportion to the severity of the skin lesions. Nevertheless, the nervous disturbances cleared up under specific therapy directed at the cutaneous, and, in some cases, the respiratory symptoms. Furthermore, in Case 4 the skin lesions were better at the time of the second visit than they were when the patient was first seen, whereas the nervousness was much worse.

Case 5 presented no skin eruption to account for the nervousness. True, there was a chronic focus of infection in the nasal sinuses which might, in a measure, have accounted for at least a part of it. However, under treatment this focus cleared up without improvement of the nervous symptoms, and it was not until the unexpected, wide-spread sensitization was found and treatment directed against this factor was instituted that improvement in his neuropathic tendencies occurred. Whether the nervous symptoms were due mainly to food, pollen or animal sensitization is purely conjectural and immaterial since we should expect that they might be the result of all these anaphylactic causes.

Cases 6 and 7 were purely nervous cases. While an anaphylactic basis for Case 7 was suggested by the history of periodic attacks of vomiting,[4] such attacks are also described as being one of the manifestations of the neuropathic diathesis. The results obtained in each case were so definite as to leave no doubt that the symptoms complained of were due to anaphylactic reactions to foods contained in the diets of the patients. In Case 8 it was possible to relieve or bring on the nervous symptoms by removing from or adding to the patient's diet the food to which she was sensitive.

That anaphylaxis might be responsible for nervousness in man through irritation of the nervous system is sound theory. Anaphylaxis is fundamentally a nervous phenomenon. Besredka emphasized this fact and founded his method for the production of shock on this principle.[5] The symptoms as seen in the experimental animal support his contention. The extreme irritability and restlessness noted immediately on injection, the scratching of the muzzle, frequently the sneezing, the dyspnea due to bronchiolar spasm, later the sudden hopping movements, and finally the convulsion itself are undisputable evidence that the nervous system is profoundly affected.

In man nervous manifestations are inseparably associated with anaphylactic phenomena. The extreme nervousness noted in individuals accompanying attacks of asthma, hay-fever, urticaria and eczema are common knowledge. Often these attacks have been attributed to

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[4] Schloss: Am. J. Dis. Child. **19**:433 (June) 1920.

[5] Besredka: Anaphylaxis and Antianaphylaxis (English Translation). 1919, C. V. Mosby Co., St. Louis, p. 13.

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THE BASAL METABOLISM OF PREMATURITY

II. RELATION OF BASAL METABOLISM TO CALORIC INTAKE AND WEIGHT CURVE *

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Scattered through the literature of basal metabolism there are isolated reports of the metabolism findings of premature infants, but up to date no series of cases has been studied consistently showing the characteristics of this type of infant.

We are presenting in this communication the basal metabolism of seven of the twenty-two premature infants studied by us during the past year and a half, in its relation to the caloric intake and the weight curves. A search of the literature gives much data in regard to the caloric intake and requirements of premature infants but in no instance have the caloric intake and the basal metabolism been recorded for the same infant.

The source of the material used was the Boston Lying-In Hospital and the Children's Department of the Massachusetts General Hospital. The subjects were all examined physically, were all organically sound, but had the characteristic appearance of premature infants, and, so far as we were able to determine, were prematurely born from one to two months.

These premature infants had high pulse rates, unstable temperatures, and were at first too weak to nurse the breast. They were consequently either fed by a Breck feeder or by tube. Breast milk was given whenever possible, but, as the supply was not unlimited, it was often necessary to supplement dilute cow's milk formulas.

They were kept in a warm premature room in which the temperature ranged between 72 and 80 F. (from 24 to 26 C.), and cared for with the usual precautions, taken with premature infants.

The blood Wassermann done on the placental blood of the mothers was, in all instances, negative.

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* From the Children's Medical Department, Massachusetts General Hospital.

These seven babies left the hospital in good condition, and some of them are still under observation.

The technic of the metabolism measurements made in this investigation was that previously described by Benedict and Talbot,[1] with some modifications. These modifications were due, primarily, to the fact that it was necessary to have a higher temperature in the respiratory chamber than was usual with older infants. Furthermore, the small size of the infants studied necessitated the measuring of smaller amounts of carbon dioxid and oxygen than were measured in larger infants. Great experimental care was taken to minimize the errors which might arise under these circumstances.

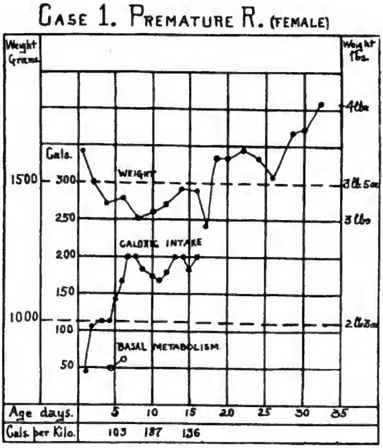

Chart 1.—Case 1. Premature R (female).

The results showed surprising conformity and we feel certain that there were no more variations in the metabolism findings than had been previously obtained in the studies of the new-born infants.[2] All possible factors were controlled, and the periods of observation were made as long as was consistent with the well being of the infant.

Charts 1 to 5, showing our findings in these subjects, were all treated in the same manner; the upper curve representing graphically the gain in weight, and the middle curve the total twenty-four hour estimated caloric food intake. This latter curve represents the food intake with as much accuracy as could be expected under the circumstances, when the food was not analyzed chemically. The lower line shows the total basal metabolism for 24 hours as measured in a respiratory chamber.

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[1] Benedict and Talbot: Carnegie Institution of Washington, D. C., Pub. No. 201.

[2] Benedict and Talbot: Carnegie Institution of Washington, D. C., Pub. No. 233.

REPORT OF CASES

Case 1 (R).—Metabolism was done on the fourth and sixth day of life and showed surprisingly low basal figures, that is, from 46 to 56 calories in twenty-four hours. The caloric intake at that time was 120 calories, or about double the basal, and, as shown by the chart, the infant continued to lose weight until the eighth day at which time he received 200 calories in the day, or more than three times the basal requirements. This figures approximately 130 calories per kilogram of body weight.

It is an open question whether the initial loss of weight would have occurred in this infant had he been able at first to digest the 200 calories he later gained on.

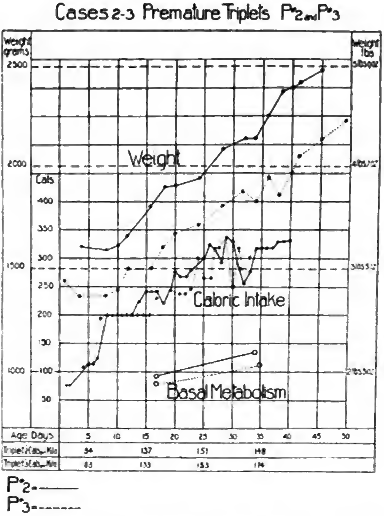

Chart 2.—Cases 2-3. Premature Tripets, P No. 2 and P No. 3

Cases 2 and 3 (P 2 and P 3).—These infants were two of triplets. They showed a corresponding similarity between their body weight and basal metabolism; the larger infant having a higher basal metabolism than the smaller infant. Both started to gain when their caloric intake reached a total of 200 calories a day; P 2 gaining on 122 calories per kilo, and P 3 on 149 calories per kilo.

These two cases serve as an excellent example of the fallacy of estimating the caloric requirements of infants per unit of body weight. A discussion of this problem will form part of a later communication. The total caloric intake of these two infants was close to two and one-half times their basal requirements on the seventeenth and thirty-fifth days of life; the calories per kilo rising very rapidly to more than 125, and, toward the end of the observed period were between 120 and 150.

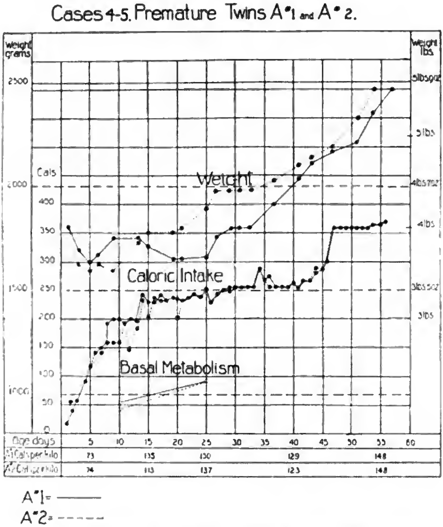

Chart 3.—Cases 4-5. Premature Twins, A No. 1 and A No. 2

Cases 4 and 5 (A 1 and A 2; twins).—These infants also had a low total basal metabolism which increased rapidly as they grew older. A 1 did not maintain a consistent gain in weight until after the twenty-fifth day of life when he was receiving a total of 250 calories or 155 calories per kilo. A 2 commenced to gain on the ninth day on a total of 200 calories, 155 calories per kilo, or about two and one-half times the basal metabolism.

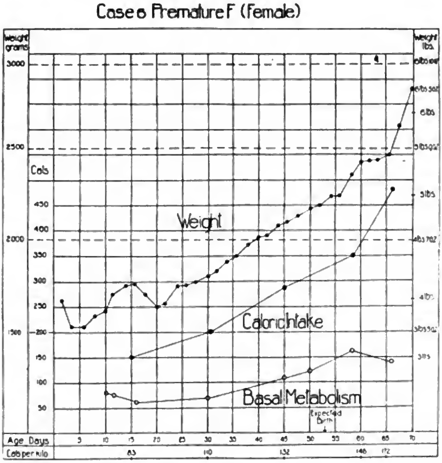

Chart 4.—Case 6. Premature F (female).

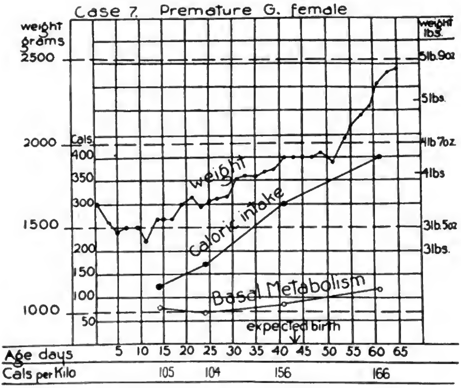

Chart 5.—Case 7. Premature G (female).

CASES 6 AND 7 (F and G).—These babies were studied over a much longer period of time and confirm the findings in the preceding cases. In Case 6 there was an increase of 71 per cent. in the basal metabolism and an increase of 230 per cent. in the caloric intake, with a resulting increase in weight of 58 per cent. over a period of fifty-one days.

In Case 7 there was an increase of 110 per cent. in the basal metabolism and an increase of 190 per cent. in the caloric intake, with an increase of 41 per cent. in the weight during the seventy days under observation.

It is interesting to note that the greater the difference between the basal requirements and the caloric intake, the greater the weekly gain in weight. There is also a tendency for the caloric intake to reach close to two and one-half times the basal findings before a satisfactory gain in weight is obtained. The record of the caloric intake in Cases 6 and 7 was recorded only a few times, at different ages, but shows that a continuous gain in weight did not result until the babies received a total of from 150 to 200 calories in the food.

Satisfactory gains in weight were not made in this series of cases until the babies were able to digest approximately 200 calories in the day. The caloric intake per kilogram of body weight was high in all cases. This is in keeping with the findings of previous investigators: Czerney and Keller, from 110 to 120 calories; Oppenheimer, Langstein and Meyer, from 120 to 130 calories; Salge, from 130 to 150 calories, and Samelson, from 115 to 150 calories.[3] J. H. Hess[4] found that infants weighing from 1,000 to 1,500 gm. had a caloric intake of from 115 to 170 calories per kilo, and infants weighing from 1,500 to 2,000 gm. had a caloric intake of from 102 to 132 calories per kilo.

The basal metabolism determinations in our series of cases was strikingly low no matter how they were charted.[5] This low metabolism seems to be dependent upon the fact that there is a very small amount of active heat forming tissues in these incompletely developed infants.

This evidence is contrary to the generally accepted belief that the heat value of the metabolism is proportional to the body surface area. Premature infants apparently only produce as much heat as is necessary for their well being in the most advantageous surroundings.

It is a well known fact that deprivation of external warmth from premature infants results in a subnormal temperature. We believe that this is evidence that the active heat forming "protoplasmic" tissues are unable to respond to the excessive heat loss from the body, and, as a result, there is a subnormal temperature; that the amount of heat formed depends on the amount and tone of the active protoplasmic tissues and not primarily on the size of the surface of the body of these infants.

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[3] Quoted from von Reuss: Die Krankheiten des Neugeborenen, Berlin, 1914.

[4] Hess, J. H.: Am. J. Dis. Child. **11**:302 (April) 1911.

[5] Talbot and Sisson: Proc. Soc. Exper. Biol. & M., April, 1922.

Close observation of premature infants shows very little muscular activity, and we have been unable to obtain any data which would lead us to suppose that the heat used up in muscular exercise in premature infants during the day was more than 10 per cent. over the basal metabolism. The loss of calories in the excreta of infants is usually less than 10 per cent. of the food intake, unless there are from four to five large curdy stools a day in which case the loss may be as high as 20 per cent. There is left, therefore, a proportionately large number of calories for growth. This is shown very well in the two cases followed over the longest period of time, that is Cases 6 and 7.

CONCLUSIONS

1. The basal metabolism in this series of premature infants was strikingly low.

2. They did not gain in weight until they were able to digest approximately 200 calories in the day.

3. The only food completely assimilated to accomplish this was human milk.

4. A relatively large proportion of the food intake goes to form new body tissue. The large excess of the caloric intake over the basal metabolism was necessary because of the relatively greater amount of growth essential for the normal development of these babies.

INFLUENZAL MENINGITIS *

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Meningitis produced by *B. influenzae*, although not extremely common, occurs frequently enough to be of considerable interest. According to Dunn[1] and Neal[2] it ranks fourth in order among the types of purulent meningitis, as shown in Table 1.

TABLE 1.—INCIDENCE OF INFLUENZAL MENINGITIS

Type of Meningitis	Dunn's Figures	Neal's Figures
Meningococcic	60	541
Pneumococcic	12	61
Streptococcic	6	49
Influenzal	4	32

In Baltimore, since 1913, at least twenty-three patients with influenzal meningitis have been seen, twenty of whom were on Dr. Howland's service in the Harriet Lane Home. Many of these cases were observed by me and I have already described[3] the biologic and serologic reactions of influenza bacilli producing meningitis. It seemed advisable to report the twenty-three cases, review the literature and try to correlate the available facts about this disease which has caused so much discussion since its recognition.

The cases reported in this paper are summarized in Table 2.

Table 3 contains a list of most of the authentic cases of influenzal meningitis on record. A number of such tables have been prepared by various workers. So many mistakes, however, were found in them that the original references have been consulted in nearly every instance. In that way the personal equation entering into the table has been limited to one person. Only infections of the meninges by *B. influenzae* alone are included in this series. When there is some doubt about the authenticity of the case, yet not enough to exclude it entirely, the fact is indicated.

Two hundred and twenty cases have been reported with seventeen recoveries (Tables 4, 5 and 6). The ages of 193 patients were given. Of these, 152 were under 2 years of age, forty-one were 2 years or older. Twelve of the seventeen recoveries, however, occurred in patients 2 years of age or older (Tables 5 and 6).

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* Received for publication, March 30, 1922.

* From the Departments of Pathology and Bacteriology, and Pediatrics, Johns Hopkins University.

TABLE 2.—SUMMARY OF TWENTY-THREE CASES OF INFLUENZAL MENINGITIS

No.	Name	Date	Age, Mos.	Spinal Fluid	Blood Culture	Leuko-cytes	Differ-ential Count	Dura-tion, Days	Primary or Secondary	Out-come	Necropsy
1	R. T.	Oct., 1913	4	B. influenzae	Negative	13,700	—	13	Primary; ears normal 3 days before death	Died	Meningitis, internal hydrocephalus; otitis; arthritis; lungs normal
2	R. C.	Nov., 1914	14	B. influenzae	Negative	22,600	—	17	Primary; ears normal on admission	Died	Meningitis; acute bronchopneumonia; otitis; mastoiditis
3	W. K.	Dec., 1915	18	B. influenzae	Negative	76,500	—	35	Primary..................	Died	Meningitis; ethmoiditis; otitis; bronchopneumonia
4	C. L.	Oct., 1916	14	B. influenzae	—	25,750	—	9	Primary..................	Died	No necropsy
5	C. M.	July, 1917	11	B. influenzae	Negative	17,600	—	23	Primary; lungs and ears clear on admission	Died	No necropsy
6	H. S.	Oct., 1917	8	B. influenzae	Negative	14,000	—	15	Secondary, possibly to pneumonia; lumbar puncture done for meningismus; diagnosis accidental	Died	Meningitis; hydrocephalus; old and new bronchopneumonia; blood culture Type IV pneumococcus
7	E. M.	Dec., 1917	7	B. influenzae	Negative	13,800	—	13	Primary..................	Died	Meningitis, cloudy swelling of liver; other organs negative
8	G. J.	Feb., 1918	2½	B. influenzae	—	42,500	—	9	Primary..................	Died	Meningitis; bronchopneumonia; cloudy swelling of kidneys; blood culture Type II pneumococcus
9	L. R.	Aug., 1918	7	B. influenzae	—	32,000	—	49	Secondary, possibly to a cold and pneumonia	Died	Meningitis; hydrocephalus; brain abscess; old and new bronchopneumonia
10	C. L.	Dec., 1918	9	B. influenzae	—	21,200	P.M.N. 82%	13	Primary; Roentgen ray Ex. Dec. 3, lungs clear; Dec. 9, pneumonia right upper lobe; diagnosis accidental	Died	Meningitis; bronchopneumonia; peritonitis; B. influenzae from brain, lungs, peritoneum; blood culture, Staphylococcus aureus
11	A. P.	Dec., 1918	16	B. influenzae	Negative	27,500	P.M.N. 87%	24	Secondary, possibly to diphtheria	Died	No necropsy
12	H. M.	Jan., 1919	7	B. influenzae	Negative	50,880	P.M.N. 80%	26	Primary..................	Died	No necropsy
13	M. H.	Jan., 1919	3	B. influenzae	B. influenzae	20,400	—	33	Primary..................	Died	Meningitis; internal hydrocephalus; sinuses, ears and mastoids clear; blood culture, sterile
14	E. L.	Apr., 1919	7	B. influenzae	B. influenzae	28,000	—	13	Primary..................	Died	Meningitis; communicating hydrocephalus; cloudy swelling of kidneys; ears, sinuses, lungs clear
15	E. T.	Aug., 1919	17	B. influenzae	Negative	20,000	—	22	Secondary, possibly to a cold and mastoiditis	Died	Meningitis; slight recent bronchopneumonia
16	M. M.	Oct., 1919	12	B. influenzae	—	16,000	—	21	Primary; ears normal; Roentgen ray Ex. o chest showed lungs normal	Died	No necropsy
17	M. S.	Nov., 1919	15	B. influenzae	B. influenzae	18,400	P.M.N. 63%	8	Secondary, possibly to cold and pneumonia	Died	Meningitis; bronchopneumonia
18	H. G.	Nov., 1919	13	B. influenzae	B. influenzae	12,200	—	—	Primary; lungs and ears clear	Recovere deaf	
19	S. D.	Jan., 1920	24	B. influenzae	B. influenzae	20,800	P.M.N. 77%	24	Primary; lungs and ears clear	Died	No necropsy
20	W. C.	Jan., 1920	8	B. influenzae	B. influenzae	21,000	P.M.N. 66%	29	Secondary, possibly to a cold and pneumonia	Died	No necropsy (developed arthritis before death)
21	M. E.	Nov., 1920	12	B. influenzae	B. influenzae	11,200	—	2	Primary; lungs and ears clear	Died	No necropsy
22	W. S.	June, 1921	10	B. influenzae	Negative	18,500	—	27	Primary; lungs and ears clear	Died	No necropsy
23	V. C.	Nov., 1921	10	B. influenzae	B. influenzae	28,300	P.M.N. 84%	12	Primary; Roentgen ray Ex. of chest showed lungs normal	Died	No necropsy

TABLE 3.—Authentic Cases of Influenzal Meningitis

Authority	No. Cases	Year Reported	Remarks
Fraenkel[4]	2	1898	
Slawyk[5]	1	1899	
Meunier[6]	1	1900	
Trailescu[7]	1	1901	
Langer[8]	1	1901	Recovery
Dubois[9]	1	1902	
Ghon[10]	1	1902	
Cagnetto[11]	2	1903-04	
Costinesco[12]	3	1903	
Mya[13]	3	1903	1 recovery*
Mya[14]	1	1903	
Thomesco and Grascoski[15]	1	1904	Recovery
Jundell[16]	2	1904	1 probable case
Bertini[17]	1	1904	
Cattaneo[18]	1	1905	
Simon[19]	1	1905	†
Dudgeon and Adams[20]	1	1907	
Sprigg[21]	1	1907	
Douglas[22]	1	1907	
Saathoff[23]	1	1907	
Adams[24]	1	1907	
Bentz and Frye[25]	1	1908	
McDonald[26]	1	1908	Probable case
Hymanson[27]	2	1909	
Cohen[28]	3	1909	
Cohoe[29]	1	1909	Recovery
Davis[30]	2	1909	1 probable case
Simon and Aine[31]	5	1910	
Simon[32]	2	1910	
Batten[33]	5	1910	1 recovery
Ager and Avery[34]	1	1910	
Ritchie[35]	3	1910	1 probable case
Sayce[36]	7	1911	1 recovery
Clemens and Gould[37]	1	1911	
Dunn[1]	4	1911	
Rhea[38]	2	1911	
Prasek and Zattelli[39]	1	1911	
Wollstein[40]	7	1911	
Brem and Zeller[41]	2	1911	
Davis[42]	5	1911	
Jundell[43]	1	1912	
Klinger[44]	4	1912	1 recovery
Henry[45]	7	1912-13	
Giese[46]	1	1913	
Drucot[47]	1	1913	Probable case
Grasty[48]	1	1913	
Ross and Moore[49]	1	1913	
Spillman and Benech[50]	1	1913	Probable case, recovery
Wollstein[51]	3	1913	
Atkinson[52]	1	1914	
Tebbutt[53]	1	1914	
Nyberg[54]	2	1915	
Ely and Weingart[55]	1	1915	
Imperatori[56]	1	1915	
Cleland and Ferguson[57]	2	1915	
Brown[58]	2	1915	
Boland[59]	1	1915	
Hill and Packard[60]	5	1915	1 recovery
Auser[61]	1	1916	
Packard[62]	1	1916	Recovery
Moody[63]	2	1916	2 probable cases
Williams[64]	1	1916	
Torrey[65]	2	1916	1 recovery
Bhat[66]	1	1917	
Tobler[67]	1	1917	
Lacy[68]	2	1918	
Hills[69]	1	1918	
Albert and Kelman[70]	1	1919	§
Johnson[71]	1	1919	Recovery
Dunn[72]	10	1920	‡
Stone[73]	1	1920	Recovery
Litchfield[74]	1	1920	Recovery
Christiansen and Kristensen[75]	3	1921	1 recovery
Finkelstein[76]	1	1921	
Abt[77]	1	1921	
Koplik	9	1921	§
Neal[3]	32	1921	1 recovery
Neal	3	1921	§
Davis	2	1921	§
Ill.	1	1922	§
Rivers	23	1922	1 recovery
Total	220	....	17 recoveries

* One of these cases also reported by Caccia.
† Reported also in 1902 and counted twice by Simon in 1910.
‡ Eleven reported, but one included under Wollstein in 1913.
§ Personal communication.

TABLE 4.—Mortality Rate

Authority	Number Cases	Number Recovered	Mortality, per Cent.
Rivers	23	1	96
Neal	35	1	97
All others	162	15	91
Total	220	17	92

TABLE 5.—Relation of Age to Incidence and to Death or Recovery in One Hundred and Ninety-Three Cases in Which Age Was Stated

Age	Number Cases	Number Deaths	Number Recoveries	Age Incidence, per Cent.	Mortality, per Cent.
Under 2 years....................	152	147	5	79	97
2 years and older..............	41	29	12	21	71

TABLE 6.—List of Recoveries *

No.	Authority	Date Reported	Age of Patient	Duration in Days	Sequels
1	Langer[8]..........	1901	9 yrs.		
2	Mya[13].......... ..	1903	9 mos.	49	Residual left facial paralysis, residual left hemiplegia
3	Thomesco and Grascoski[15]....	1904	7 yrs.	10	
4	Cohoe[29]..........	1909	33 yrs.	15	
5	Batten[33].........	1910	14 mos.	30	Partial blindness, difficulty in sitting and walking
6	Sayce[36]...........	1911	4 yrs.		
7	Klinger[44].........	1912	26 yrs.	60	
8	Spillman and Benech[50].......	1913	Adv. age	14	
9	Hill and Packard[60]...........	1915	4 mos.	20	
10	Packard[62].......	1916	11 yrs.	17	
11	Torrey[63].........	1916	11 yrs.	20	
12	Johnson[71].......	1919	3 yrs.		
13	Stone[73]..........	1920	15 yrs.	11	Double optic neuritis with some residual blindness; some residual involvement of third nerve on one side
14	Litchfield[74]......	1920	23 mos.	70	
15	Christiansen and Kristensen[75]...	1921	2 yrs.	23	
16	Neal[2].............	1921	2½ yrs.	30	
17	Rivers............	1922	13 mos.	..	Complete nerve deafness

* Twelve of seventeen recoveries, 71 per cent., occurred in patients 2 years of age or older.

CLINICAL PICTURE

The diagnosis of meningitis of all kinds is difficult in infants and young children. Influenzal meningitis is no exception. The 220 cases on record must be only a few of those diagnosed, and the number recognized does not necessarily include all that actually occurred. Batten [33] agrees with me that many are overlooked.

There is no group of clinical findings peculiar to influenzal meningitis. At times it is indistinguishable clinically from epidemic cerebrospinal meningitis. A hemorrhagic rash [2] even may be present which is supposed to be characteristic of the latter disease. It may simulate tuberculous meningitis, as an extreme bulging of the fontanel, paralysis of the eye muscles and irregular respirations (atypical Cheyne-Stokes) are frequently seen in patients living many days. Henry [45] reported the spontaneous rupture of the fontanel in an infant 10 months of age. A strabismus was seen at some time in ten of my twenty-three patients. Paralysis of the face or extremities, arthritis, deafness and blindness occur in the order mentioned. The temperature may be elevated continuously or irregularly. Febrile periods may alternate with periods of normal temperature (see temperature charts accompanying the abstracts of case records). Influenzal meningitis is most commonly mistaken for pneumonia and this is probably due to an unexplained fever associated with rapid, difficult or embarrassed respirations.

White Blood Cell Count.—A leukocytosis with an increase in the percentage of the polymorphonuclear cells is usual (Table 7). Influenzal meningitis, a pure infection with Pfeiffer's bacillus, has an entirely different blood picture from the one seen in epidemic influenza which is accompanied by a leukopenia.

TABLE 7.—White Blood Cell Count in Influenzal Meningitis

	White Blood Cells per C. Mm.				Per Cent. Polymorphonuclear Cells	
Authority	No. Cases	Low	High	Average	No. Cases	Average
Rivers	23	11,200	76,500	24,499	7	77
All others	17	7,600	38,000	17,018	10	78
Total	40	7,600	76,500	21,320	17	78

The figures show that a polymorphonuclear leukocytosis is usually present in influenzal meningitis.

Blood Cultures.—In eighteen of my cases records of antemortem blood cultures are available (Table 2). Eight, or 44 per cent., were positive for *B. influenzae.* Most of the positive results were obtained from the patients listed in the last half of the table. So many negative results in the first half may have been due to inability to grow the bacilli when present. Records of antemortem and postmortem blood cultures were found in twenty-four instances in the review of the literature. Sixteen were positive for influenza bacilli.

Spinal Fluid.—Early in the disease the spinal fluid is slightly turbid with a ground-glass appearance. Usually polymorphonuclear cells predominate. Later the fluid may become so purulent and thick that it often flows with great difficulty or not at all through the needle. Batten [33] believes that a very purulent fluid is more or less indicative of influenzal meningitis. Smears of the fluid practically always show many gram-negative pleomorphic bacilli, usually extracellular. No difficulty should be experienced in obtaining cultures of these bacilli when the proper medium is used.[78] An indole test on the spinal fluid, as described by Rivers,[79] is an aid in rapid diagnosis. While the bacilli are easily demonstrated in direct smears or in cultures by one accustomed to working with them, they may be overlooked by one less experienced. Consequently, some cases of influenzal meningitis may be treated as meningococcus infections in which no organisms were seen or grown and tabulated as deaths from epidemic cerebrospinal meningitis.

Duration.—A false impression of the duration of the disease may be obtained from a few cases. Death may come quickly, in from twenty-four to thirty-six hours, or the patient may linger for days or months. Sayce[36] reported that a child, 5 years old, lived six months after the diagnosis of influenzal meningitis had been established. Eighteen lumbar punctures were made at various times and *B. influenzae* was isolated. At the necropsy these findings were confirmed. Many patients lived twenty, thirty, forty or sixty days. The average duration of the disease in thirty-two of Neal's patients was sixteen days; in Rivers' twenty-two cases, twenty days; in 112 cases, all others, eighteen days. The average for these three groups, comprising 166 patients, was eighteen days. The duration of the disease in the patients who recovered was given in thirteen instances (Table 6). The average was twenty-eight days.

Sequels.—Four of the seventeen recoveries were not complete (Table 6). Blindness, paralyses and deafness are the usual sequels.

NECROPSIES

The pathologic findings at necropsy depend a great deal on the duration of the disease before death. This is well illustrated by Rhea's[39] two cases. The first patient was an infant 6 months old which died after an illness of three days. The necropsy revealed an acute hemorrhagic meningitis and encephalitis, an acute pharyngitis, laryngitis and bronchopneumonia. The heart's blood was sterile. A pure culture of influenza bacillus was obtained from the meninges and the bacilli were also seen in the exudate in the sections of the meninges. The encephalitis may explain some of the paralyses reported. The second patient was a child 5 years of age which became sick suddenly. Influenza bacilli were obtained in pure culture from the spinal fluid and the blood. Before death, which came after an illness of eighty-nine days, a left hemiplegia and signs of hydrocephalus developed. An organizing meningitis with thickening and thrombosis of many of the blood vessels, and an internal hydrocephalus were found at necropsy. The ears, sinuses and lungs were normal. Cultures from the meninges and heart's blood remained sterile. These two cases are probably the extremes of the pathologic picture, which is usually one of a massive purulent meningitis. The exudate may collect at the base, along the vessels or in patches over the cortex. At times, the whole brain seems to be wrapped in a layer of pus 2 mm. thick. Hydrocephalus is common. A brain abscess has been observed twice (Davis;[42] Rivers). Bronchopneumonia is found in a large number of the patients. Otitis media, sinusitis, arthritis, peritonitis, nephritis and cloudy swelling of the liver and kidneys are some of the findings in other parts of the body.

ABSTRACTS OF CASE RECORDS

Abstracts of eight case records are given to illustrate many points already mentioned and to emphasize others that will be considered later.

CASE 1 (1).—R. T., colored boy, 4 months old, became ill Oct. 20, 1913, with a "pain in the stomach" and loose bowels. These symptoms increased somewhat in severity until October 28, when the mother noticed while bathing and dressing the child that the left shoulder was tender. There was no history of a cough, vomiting or convulsions. Drowsiness was noticed for the first time October 30, the day of admission to the hospital. The physical examination on admission showed a stiff neck, retracted head, hyperesthesia, no discharge from the nose, normal ear drums, atypical Cheyne-Stokes respirations, normal lungs and heart, spastic paralysis of the left arm, no arthritis of the left shoulder or elbow, swelling of the left wrist and exaggerated deep reflexes. Kernig's sign was present. The white blood cell count was 13,760. The spinal fluid was cloudy. Gram-negative bacilli were seen in smears of the spinal fluid. Culturally these were influenza bacilli. The blood culture remained sterile. November 1 an internal strabismus of the right eye and a fluctuation in the swelling of the left wrist were noticed. A second blood culture made at this time also remained sterile. The patient died November 2, after an illness of thirteen days.

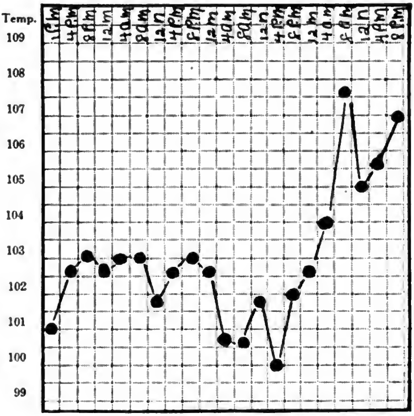

Fig. 1.—Temperature Chart for Case 1.

Anatomic Diagnosis (Necropsy 4015).—Fibropurulent cerebrospinal meningitis, internal hydrocephalus, suppurative otitis media (right), suppurative arthritis of left wrist, focal necrosis of liver, thrombosis of portal vein, pseudo-infarction of liver.

Remarks.—The intern obtained no history of a respiratory infection preceding the illness. Intestinal symptoms predominated at the onset. After the diagnosis of influenzal meningitis was made, however, the resident managed to secure from the mother some kind of an indefinite history of a "cold" from which the child had suffered. The temperature chart would pass for that of a patient with tuberculous meningitis. No portal of entry was found at necropsy unless it were the otitis media, but the ear drums were normal to otoscopic examination three days before death.

Case 2 (5).—C. M., colored girl, 11 months old, refused to eat, had fever and held her head retracted, July 13, 1917. She would not use her right arm as before. Two days later the mother noticed a "cap" (bulging fontanel) on the baby's head. The patient was admitted to the hospital July 17.

The physical examination on admission showed a conscious, irritable, hyperesthetic. rachitic child with a stiff neck and bulging fontanel, an internal strabismus of the left eye, no discharge from the nose, normal ear drums, and no definite signs of pneumonia. Kernig's sign was absent. The right arm was used less than the left. The white blood cell count was 17,600. A tentative diagnosis of tuberculous meningitis was made. The spinal fluid was slightly turbid with a cell count of 750 per c. mm. About half of the cells were mononuclears. Films formed but no tubercle bacilli were found. Other organisms were not looked for or were missed. Cultures were not made at this time. July 31 another lumbar puncture was made to search for tubercle bacilli. At this time gram-negative bacilli were seen and properly identified as *B. influenzae.* Another examination of the spinal fluid, August 3, confirmed the diagnosis of influenzal meningitis. A blood culture made August 1 remained sterile. The respirations became irregular, atypical Cheyne-Stokes. Definite signs of pneumonia developed before death, which occurred August 5. A necropsy was not allowed.

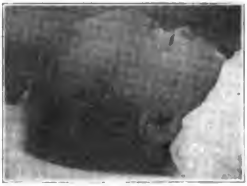

Fig. 2.—Photograph showing the bulging fontanel in Case 5.

Remarks.—This illustrates how easily influenzal meningitis can be mistaken for tuberculous meningitis. From the history and the course in the hospital nothing to which the meningitis could have been secondary was found. The pneumonia developed after the patient came into the hospital.

Case 3 (7).—E. M., white girl, 7 months old, refused to nurse Dec. 8, 1917. She remained in a stupor for twenty-four hours, after which she began to have convulsions. These convulsions, five or six a day, involved only the right side of the body and persisted until admission to the hospital, December 17. The mother noticed that the head was retracted December 16.

The physical examination on admission showed a retracted head, no discharge from the nose, slightly reddened ear drums, normal lungs, and constant twitchings of the right arm and leg. Kernig's sign was present. White blood cell count was 13,800. The spinal fluid was cloudy and contained gram-negative bacilli which were influenza bacilli culturally. The blood culture remained sterile. Roentgen-ray examination of the lungs on the day of admission showed that they were practically normal. Temperature ranged between 101 and 103 F. most of the time, but dropped nearly to normal before death, December 21.

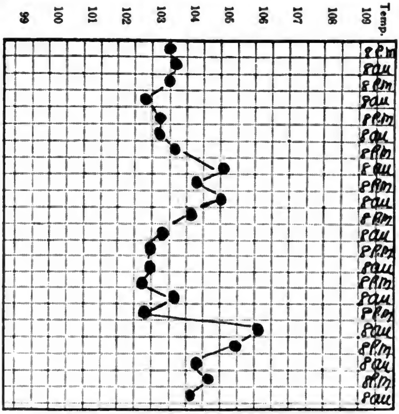

Fig. 3.—Temperature Chart for Case 5.

Anatomic Diagnosis (Necropsy 5396). — Purulent cerebrospinal meningitis, cloudy swelling of the liver.

Remarks.—There is nothing in the history, physical examination, course in the hospital, or in the necropsy findings to suggest that this was anything other than a primary influenzal meningitis.

Case 4 (8).—G. J., colored girl, 2½ months old, became drowsy, refused to nurse and "rolled eyes up," Feb. 26, 1918. She gradually became worse and would scream when touched. March 4 the child began to have convulsions and was admitted to the hospital the next day.

The physical examination on admission showed a bulging fontanel, retracted head, stiff neck, internal strabismus of the left eye, no discharge from the nose or ears, few râles in the lungs, palpable spleen and exaggerated deep reflexes. Kernig's sign was present. White blood cell count was 42,500. The spinal fluid was cloudy and contained gram-negative bacilli which culturally were influenza bacilli. Patient died March 7.

Anatomic Diagnosis (Necropsy 5473).—Massive purulent cerebrospinal meningitis, acute splenic tumor, cloudy swelling of the kidneys, bronchopneumonia, fibrous pleural adhesions (bilateral).

Necropsy Bacteriology.—Culture from meninges showed only *B. influenzae.* Culture from heart's blood showed only pneumococcus Type II.

Remarks.—The patient was afebrile while in the hospital. As far as can be determined, this is an example of a primary influenzal meningitis. Only small areas of bronchopneumonia were found in the lungs. The Type II pneumococcus found in the blood at the necropsy is interesting. Fixed types of pneumococci usually produce lobar pneumonia. They can, however, under the proper conditions act as secondary invaders and even cause bronchopneumonia.

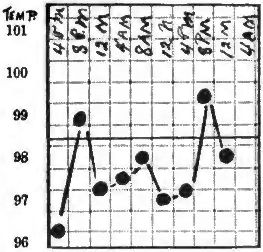

Fig. 4.—Temperature Chart for Case 8.

Case 5 (12).—H. M., white female, 7 months old, became drowsy and feverish three weeks before admission to the hospital. At first there was a slight discharge from the nose. The family physician treated the baby for bronchitis in spite of the fact that she had no signs of it, not even a cough until a few days before coming to the hospital. One week before admission projectile vomiting after each feeding developed and three days before admission the head became retracted. The patient was admitted Jan. 21, 1919.

The physical examination showed a conscious, hyperesthetic baby with a stiff neck and a retracted head, no discharge from the nose or ears, anisocoria, indefinite signs of pneumonia in right interscapular region, exaggerated deep reflexes. White blood cell count was 50,880. The spinal fluid was very thick and purulent. Gram-negative bacilli were seen in the smears. Culturally, these were influenza bacilli. The blood culture remained sterile. The child gradually became worse and began to have numerous convulsions before she died January 26. A necropsy was not allowed.

Remarks.—The child probably had a meningitis from the beginning. It was primary as far as can be determined. In spite of a purulent meningitis the temperature was normal for two days after admission to the hospital. The rise in temperature several days before death cannot be accounted for definitely. There are two possibilities, a terminal rise before death that is seen not infrequently in meningitis, or the development of a pneumonia.

Case 6 (14).—E. L., white boy, 7 months old, became irritable April 4. 1919. He gradually grew worse and would scream when touched or handled. Stiffness of his neck was noticed April 8, two days before admission to the hospital.

Physical examination when first seen showed a conscious child with a bulging fontanel, retracted head and stiff neck, no discharge from the nose, normal ear drums, normal lungs, and paralysis of the right arm. Kernig's sign was absent. White blood cell count was 28,000. The spinal fluid was cloudy. Gram-negative bacilli were seen in the smears. Culturally these were influenza bacilli. From the blood culture influenza bacilli were obtained also. April 10 it was noticed that the paralysis of the right arm had disappeared. The child gradually became worse. Before death, which occurred April 17, convulsions set in and an external strabismus of the right eye was seen.

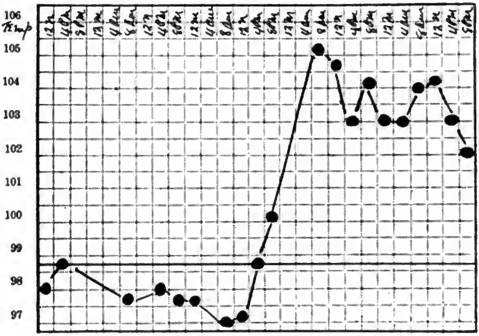

Fig. 5.—Temperature Chart for Case 12.

Anatomic Diagnosis (Necropsy 5880). — Purulent cerebrospinal meningitis, communicating hydrocephalus, cloudy swelling of the kidneys.

Remarks.—The ears, sinuses and lungs were normal while in the hospital and at necropsy. Influenza bacilli were obtained from the spinal fluid and blood during life and from the meninges and heart's blood at necropsy. The bacilli were pathogenic for rabbits.

Case 7 (18).—H. G., white girl, 13 months old, became irritable and "droopy" Nov. 24, 1919. No history of vomiting, convulsions or rigidity was obtained. An internal strabismus of the left eye appeared November 26, the day before the patient was brought to the hospital.

Physical examination showed a conscious, irritable, restless child that would not sit or stand as formerly, tense fontanel, internal strabismus of left eye, no discharge from the nose, normal ear drums, normal lungs. Kernig's sign absent. White blood cell count was 12,200. The spinal fluid was cloudy. Gram-negative bacilli were found in the smears. The organisms were

B. influenzae culturally. Influenza bacilli were obtained from the blood culture. The patient was taken home November 28. The child was a private patient of Dr. Hamburger. He reported later that she had recovered but was completely deaf.

Remarks.—There is nothing in the history, physical examination, or course of the disease to obviate the possibility that this might have been a primary influenzal meningitis. The organism was pathogenic for rabbits.

Case 8 (19).—S. D., white girl, 2 years old, suddenly developed fever and irritability Jan. 13, 1920. Three days later the neck became stiff. An internal strabismus of the left eye was noted January 18, the day of admission to the hospital.

Physical examination on admission showed a conscious child that would answer questions, but had a stiff neck, internal strabismus of the left eye, no discharge from the nose, normal ear drums, normal lungs. Kernig's sign was present. White blood cell count was 20,800. The spinal fluid was cloudy. Gram-negative bacilli were seen in the smears. The organisms were *B. influenzae* culturally. Influenza bacilli were obtained from the blood culture. During the first twelve days in the hospital the patient did not seem very sick. She would eat, move around the bed and talk. Then she began gradually to become more ill until she died February 6. The spinal fluid became so thick toward the last that it would not run through the needle. No signs of pneumonia were made out at any time. Six days before death the right ear drum became inflamed. A necropsy was not allowed.

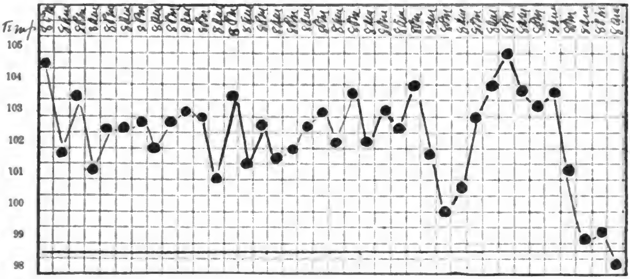

Fig. 6.—Temperature Chart for Case 19.

Remarks.—This is another example, as far as can be determined, of a primary influenzal meningitis. The right ear drum became inflamed eleven days after the patient came to the hospital, about the time she became much worse and when under less favorable conditions the meningitis might have been recognized for the first time. No doubt many infections of the middle ear reported in connection with influenzal meningitis and thought of as possible portals of entry have occurred late in the course of an unrecognized meningitis.

This clinical picture is well known. Nothing further can be gained by reporting cases as they occur. The main interest is centered around the question of whether influenzal meningitis is a primary or a secondary disease. No attempt will be made to tabulate all the ideas on the subject expressed by various workers. It seems they can be divided into three main groups. Under each of these will be given a few specific references.

DIFFERENT CONCEPTIONS REGARDING NATURE OF INFLUENZAL MENINGITIS

1. *Secondary to a Respiratory Infection.*—Many clinicians thought and still believe that *B. influenzae* is the cause of epidemic influenza. Naturally these observers would conclude that influenzal meningitis is a complication of a respiratory infection. Wollstein [40] and Dunn [72] are of that opinion. Flexner [50] said, "It is probable that the infection of the meninges is always secondary to the respiratory infection." Hill and Packard [60] stated that the portal of entry was through the respiratory tract, secondary to influenza.

2. *Part of a Generalized Infection.*—Dudgeon and Adams [20] considered the meningitis a part of a metastatic pyemic condition. Cohen [28] also thought that the meningitis was a part of a generalized infection. He believed, however, that this infection was caused by a definite group of organisms which he claimed differed from Pfeiffer's bacillus and called them *Bacille méningite cérébrospinale septicémique.*

3. *A Primary Meningitis.*—Klinger [44] hinted that influenzal meningitis might be a primary idiopathic disease similar to epidemic cerebrospinal meningitis and was so bold as to suggest that the patients be isolated and that some kind of disinfection be observed in connection with them. Nyberg [54] thought that one of his patients had a primary influenzal meningitis caused by one of a group of influenza bacilli having a predilection for the meninges.

The pathogenesis of influenzal meningitis will not be discussed in this paper further than to state that one's ideas in regard to it might vary, depending on whether it proves to be a primary or a secondary disease. Consequently all the evidence possible has been collected to determine whether any definite conclusions about the latter question can be reached.

INFORMATION FROM HISTORIES AND NECROPSIES

Histories.—The records of cases of influenzal meningitis reported in the literature and of the twenty-three cases in my series have been analyzed to discover what evidence they may provide as to the primary or secondary nature of the disease. With the exception of Neal's [2] thirty-two cases, my judgment is a large factor in Tables 8 and 9.

Observers reporting cases have gone out of the way to find some preceding infection to which the meningitis might have been secondary. This is well illustrated by Case 1 in my series. In certain instances it is fairly evident that the meningitis was overlooked for a long time, often until after an otitis media, an arthritis, or a pneumonia had been found. In some instances, the minority, however, the meningeal infection was undoubtedly secondary, particularly to mastoiditis. Three of Henry's [45] patients who were operated on for acute mastoid infections are good examples. Unfortunately, two of them have to be omitted as the meningitis was caused by two organisms—hemolytic streptococci and influenza bacilli. Other examples of secondary infections have been reported by Packard [62] and Imperatori.[56] In 171 instances (Table 8) it was possible from the history and course of the disease to form some opinion as to whether the meningitis was primary or secondary.

TABLE 8.—Division of One Hundred and Seventy-One Cases, from Their Histories, Into Possible Primary and Possible Secondary Infections

Authority	Number Cases	Number Primary	Number Secondary	Per Cent. Primary	Per Cent. Secondary
Rivers	23	17	6	74	26
Neal	32	24	8	75	25
All others	116	86	30	74	26
Totals	171	127	44	74	26

Necropsies.—Bronchopneumonia was found in the majority of the cases at necropsy. Immediately the question arises as to whether the pneumonia was complicating the meningitis or vice versa. Bertini [17] and Davis [42] state that they could not be certain whether the pneumonia antedated the meningitis in their cases or not. Giese,[46] in reporting a case of influenzal meningitis, said that the meningitis was primary and that the slight pneumonia present was secondary. Torrey [65] and Tobler [67] suggested that the influenza bacilli pass from the cerebrospinal space into the circulation, giving rise to secondary infections in other organs. It is also possible that some of the pneumonia in these cases is caused by pneumococci or streptococci, similar to that occurring in children with dysentery or severe diarrheas. Christiansen and Kristensen [75] reported that they recovered from the meninges of a patient dead of influenzal meningitis a pure culture of influenza bacilli and from the pneumonic consolidation in the lungs a pure culture of pneumococci. From two of my patients (Nos. 6 and 8) evidence was obtained that other bacteria might cause some of the complications found at necropsy. These patients had bronchopneumonia in addition to a meningitis. A pure culture of influenza bacilli was obtained from the meninges of both cases, while from the heart's blood of one case a pure culture of a Type IV pneumococcus was recovered and from the heart's blood of the other a pure culture of a Type II pneumococcus was recovered. Unfortunately, cultures from the lungs were not made or the results were not recorded.

Necropsies were obtained in twelve of the twenty-two fatal cases in my series. In three of these twelve, 25 per cent., meningitis alone was found. The ears, sinuses, and lungs were normal. If there was a primary focus, it was overlooked or it had healed. The patients had been sick eleven, thirteen and thirty-three days, respectively. From the literature records of seventy-one necropsies, many of which were partial, have been examined. Often the findings in the brain were given without stating whether the other organs were normal or not examined. In spite of these difficulties, however, records of ten cases were seen in which a meningitis alone was found. The number of possible primary cases of influenzal meningitis observed at necropsy are listed in Table 9. If these figures are correct, it would be easy to assume that many more were primary also, the pneumonia and other pathologic lesions complicating the meningitis.

TABLE 9.—THE NUMBER OF POSSIBLE PRIMARY CASES OF INFLUENZAL MENINGITIS AS DETERMINED BY SEVENTY-ONE NECROPSY RECORDS

No. Cases	Necropsy Findings	Per Cent.
10	Meningitis alone	14
1	Meningitis, peritoneal fluid contained B. influenzae, blood culture sterile, lungs, ears, and sinuses normal	
1	Meningitis, peritonitis (B. influenzae), blood culture sterile, lungs normal	
3	Meningitis, lungs normal	
2	Meningitis, lungs and ears normal	27
3	Meningitis, otitis media	
1	Meningitis, pericarditis, endocarditis	
2	Meningitis, arthritis	
1	Meningitis, bronchopneumonia (pure culture pneumococcus)	
5	Meningitis, small patches of bronchopneumonia which in some instances was suggested as being secondary	
29	Total possible primary cases	41

Possibility of Spread by Carriers.—So few cases of influenzal meningitis occur that it is impossible to show that the disease is spread by contact. There are facts, however, that might make one think that it is spread by carriers. Many observers report several cases occurring within a short time of each other. Hill and Packard[60] saw four cases in six months. Henry[45] observed at least five cases in 1910. In Dr. Howland's clinic seven cases were seen in one year. Simon and Aine,[31] in reporting five cases, speak of them as a little epidemic of influenzal meningitis. Davis[30] reported that twins 5 days old became ill at the same time, one died on the ninth day, the other on the twelfth. At the necropsy the first one was found to have had an influenzal meningitis. No lumbar puncture or necropsy was made in the second case.

Although there may be some doubt about the second child having a meningitis, yet it is reasonable to suppose that it did, as it became ill at the same time and ran a course similar to the other. Davis[42] also reported two cases of influenzal meningitis that occurred in a small institution of about fourteen inmates. The second child became ill two weeks after the death of the first. While not convincing, the evidence is at least suggestive that influenzal meningitis is a carrier-borne disease.

Incubation Period.—Enough information is not available to draw any conclusions in regard to the length of the incubation period. In the case of Davis' twins, however, one can be certain that the incubation period was not longer than five days.

Yearly Incidence of Influenzal Meningitis.—Jordan[81] and Neal[2] have commented on the fact that there was no great increase in influenzal meningitis during and after the pandemic of influenza in 1918. This was used to show that there is no definite relationship between the etiology of the two diseases. Table 10 and Figure 7 give the incidence of influenzal meningitis by years in 203 instances where the year was stated or could be approximated.

TABLE 10.—Yearly Incidence of Two Hundred and Three Cases of Influenzal Meningitis

	Number of Cases				Number of Cases		
Year	Year Stated	Year Approximated	Total	Year	Year Stated	Year Approximated	Total
1897	2	0	2	1910	21	6	27
1898	0	0	0	1911	6	2	8
1899	2	1	3	1912	9	2	11
1900	0	0	0	1913	5	2	7
1901	0	2	2	1914	9	0	9
1902	8	3	11	1915	11	4	15
1903	2	3	5	1916	9	0	9
1904	0	0	0	1917	12	0	12
1905	1	1	2	1918	12	0	12
1906	3	0	3	1919	18	0	18
1907	10	0	10	1920	10	0	10
1908	8	0	8	1921	6	0	6
1909	6	7	13				
Total					170	33	203

Regardless of the etiology of epidemic influenza it would be difficult for one to deny an increased prevalence of *B. influenzae* during the last pandemic of that disease. With this increased prevalence of influenza bacilli and with so much disease of the respiratory tract there should have been a decided increase in the number of cases of influenzal meningitis if the ordinary respiratory strains of *B. influenzae* were the usual cause of the latter disease. From Table 10 and Figure 7 it is evident that there was no marked general rise in the number of cases. In Chicago, according to Jordan[81] and Davis,[82] there was practically no influenzal meningitis. In New York, according to Neal,[2] only one case occurred during the epidemic of influenza in the autumn of 1918. There was, however, a slight rise in the number of cases for 1916, 1917, 1918 and 1919. In Baltimore, on the other hand, there was a decided increase during 1917, 1918, 1919 and 1920 (Fig. 7). In spite of this increase in the number of cases, no definite relationship between influenza and influenzal meningitis can be discovered as the majority of the cases of the latter disease did not occur during the epidemics of the former. All one can say is that in different localities there is a fluctuation in the number of cases of influenzal meningitis from year to year and that this fluctuation is not dependent on epidemic influenza.

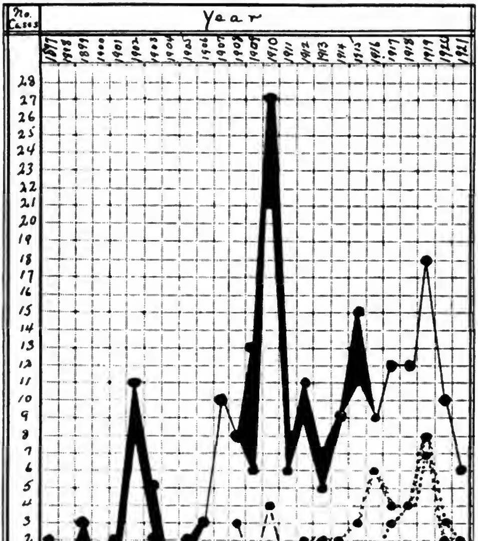

Fig. 7.—The unbroken line shows the yearly incidence of 203 cases of influenzal meningitis. The lower level of the shaded areas represents the number of cases that were stated as occurring in that year, the upper level represents the above cases plus the ones in which the year of occurrence was approximated. — — — —, yearly incidence in Chicago of cases seen by Davis; ...., yearly incidence of Rivers' cases in Baltimore; x x x x, yearly incidence of Neal's cases in New York City.

The year of occurrence can be approximately stated in 203 instances of influenzal meningitis (Table 10 and Fig. 7). The striking thing is that the greatest number in one year was in 1910 when the world was exceptionally free of epidemic and interepidemic influenza.[83] A possible explanation for this will be apparent when the biologic and the serologic reactions of the meningitic and respiratory strains of *B. influenzae* are compared.

Seasonal Incidence of Influenzal Meningitis.—The month of occurrence of the cases of influenzal meningitis was stated in 126 instances. Most of them were in October, November, December and January (Fig. 8). In Baltimore pneumonia is more prevalent after Christmas, while influenzal meningitis (Fig. 8) occurs more frequently during the months just before Christmas, prior to the pneumonia season. In New York the majority of Neal's[2] cases occurred also during the months of October, November, and December (Fig. 8). Holt[84] has pointed out that in New York the curve of tuberculous meningitis, plotted by months, follows the curve of deaths from pneumonia (Fig. 8). The peaks of these curves come well after Christmas, in March and April. The etiology of tuberculous meningitis cannot be confused with that of ordinary pneumonia. Holt suggested that the curves parallel each other because acute respiratory diseases cause an exacerbation and a dissemination of tuberculosis. On the other hand, the curve of influenzal meningitis, which has been considered by many to be secondary to acute respiratory infections, does not follow the curve of deaths from pneumonias as closely as does tuberculous meningitis (Fig. 8).

Biologic and Serologic Reactions of Different Influenza Bacilli.—If influenzal meningitis be a primary disease in most instances, one would expect to find a close relationship culturally and serologically between the strains producing it. Povitsky and Denny[85] demonstrated that four of seven meningitic strains were identical by absorption of agglutinin tests. Rivers and Kohn,[3] working with thirteen strains of influenza bacilli isolated from the meninges or the spinal fluids of patients with influenzal meningitis, showed that eleven were alike culturally. These eleven strains were closely allied, as shown by agglutination tests. By absorption of the agglutinin test two main groups were found: Group I of seven strains; Group II of three strains, an intermediate group of one strain. At that time four blood culture strains isolated from children with pneumonia following influenza were studied also. These were found to be different from each other and from the meningitic strains. Since the publication of that paper two more meningitic strains have been studied, one of which fell into Group I, the other was identical with none of the other strains. This grouping of the meningitic strains is especially marked in distinction to the apparent heterogeneity of the respiratory strains as shown by Valentine and Cooper,[86] Povitsky and Denny,[85] Chesney,[87] and others.

I have compared the meningitic strains with fourteen respiratory ones other than the four blood culture strains already mentioned. In no instance was any one of the respiratory strains identical with the meningitic strains serologically, even when they had similar cultural characteristics. If influenzal meningitis proves to be a carrier-borne disease, however, meningitic strains will be found eventually in throat cultures. In all, fifteen meningitic strains have been studied, eight of which were in Group I, three in Group II, one intermediate, and three heterogeneous strains. Of eighteen respiratory strains none was found identical with the meningitic strains. These results are summarized in Table 11.

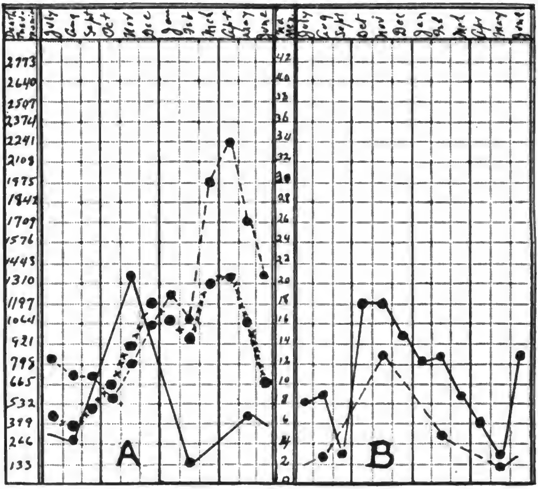

Fig. 8.—A. x x x x, seasonal incidence of deaths from pneumonia in New York City for one year. — — — —, seasonal incidence of 218 cases of tuberculous meningitis in New York City. ———, seasonal incidence of thirty-five cases of influenzal meningitis in New York City. The two upper curves were copied from Holt.[84] The lower curve was plotted from Neal's[2] figures.

B. ———, seasonal incidence of 126 cases of influenzal meningitis. — — — —, seasonal incidence of Rivers' twenty-three cases of influenzal meningitis.

From four of the patients with a meningitis blood culture strains were obtained and studied also. These were found to be identical with the corresponding meningeal strains. This is contrary to the findings of Anderson and Schultz,[88] who reported that the meningeal and the blood culture strains from the same patient were different immunologically.

The fact that most of the meningitic strains of *B. influenzae* are different from the respiratory ones probably accounts for the absence of a marked increase in the prevalence of influenzal meningitis during the pandemic of influenza when influenza bacilli were plentiful in diseased respiratory tracts.

Relative Pathogenicity of Meningeal and Respiratory Strains.—Cohen,[28] and Cohen and Fitzgerald [89] were among the first to suggest that *B. influenzae* from patients with meningitis differed from ordinary respiratory influenza bacilli. They based their conclusions on results of agglutination tests, protection experiments, and on the fact that the meningitic strains were highly pathogenic for rabbits. Wollstein,[40] from her studies concluded that respiratory and meningeal strains of *B. influenzae* were more or less identical culturally and immunologically, varying only in virulence.[90] She [51] has shown conclusively, however, that there is a difference between the two groups in the pathogenicity for rabbits. Of seventy respiratory strains only four were pathogenic for rabbits, while eight of nine meningitic strains were pathogenic. Davis [42] failed to find any difference in the virulence of respiratory and meningeal strains. Other observers have usually found the meningeal strains pathogenic for small animals, especially rabbits. Henry [45] isolated from one of his patients with influenzal meningitis a bacillus that was nonpathogenic for laboratory animals. He obtained pathogenic bacilli, however, from some of his other patients. The nonpathogenic

TABLE 11.—Summary of the Biologic and the Serologic Reactions of Fifteen Meningitic and Eighteen Respiratory Strains of B. Influenzae

	Biologic Reactions					Groups Determined by Absorption Tests		
No. Strains	Nitrate Reduction	Indol Formation	Glucose	Xylose	Maltose	Group I	Intermediate	Group II
Meningitic								
8	+	+	+	+	—	+	—	—
1	+	+	+	+	—	—	+	—
3	+	+	+	+	—	—	—	+
1	+	—	+	+	—	—	—	—
1	+	+	+	—	—	—	—	—
1	+	+	—	—	—	—	—	—
Respiratory								
7	+	+	+	+	—	—	—	—
4	+	+	+	—	—	—	—	—
5	+	—	+	+	—	—	—	—
1	+	—	+	+	+	—	—	—
1	+	—	+	—	+	—	—	—

+ indicates nitrates are reduced and indol is formed; — indicates the oppposite. Under the sugars + indicates acid is formed without gas; — indicates neither acid nor gas is formed. Under grouping + indicates into which group the strains fall; — indicates that the strains do not belong to that group.

organism was isolated from a patient with a meningitis following a mastoiditis for which an operation was done. At the necropsy the meningitis was localized mostly at the base and on the side of the brain near the site of operation. Perhaps this was an instance of a secondary meningitis produced by an ordinary respiratory strain of *B. influenzae*. In that event the bacillus would be expected to have the pathogenicity as well as the serologic reactions of an ordinary respiratory strain. I have tested the pathogenicity of five meningeal strains and found that all of them, when first isolated, killed rabbits in small intravenous doses. The few respiratory strains so far tested have failed to do so.

DISCUSSION

The facts in this paper are not presented as conclusive evidence that influenzal meningitis in the majority of instances is a primary disease. They are suggestive enough, however, to indicate that such may be the case and to show how the disease should be thought of and studied in the future. The idea that it is a primary disease caused by the special group of *B. influenzae* does not exclude the possibility that it may at times be secondary and produced by ordinary respiratory strains of influenza bacilli, nor does it exclude the possibility that the meningitic strains may occasionally produce diseases other than meningitis.

Treatments of various kinds have been used, but as far as can be determined none has accomplished much. Even the serum[72] produced by Wollstein[91] has not given the results expected.[51] It may be, since more is now known of the biologic and the serologic reactions of meningitic strains of influenza bacilli, that a better treatment serum can be produced.

SUMMARY

The records of 197 cases of influenzal meningitis have been reviewed and twenty-three new cases are reported.

Influenzal meningitis is a disease of infancy, 79 per cent. of cases occurring in patients under 2 years of age.

The mortality in 220 cases was 92 per cent. Of the seventeen patients who recovered twelve were 2 years of age or older.

There is no typical clinical picture of influenzal meningitis. Many cases are probably overlooked.

There is usually a polymorphonuclear leukocytosis.

From the case records it is possible to say that the meningitis might have been primary in the majority of instances.

Influenzal meningitis is probably a carrier-borne disease.

The seasonal and yearly incidence of influenzal meningitis and of epidemic influenza and pneumonia do not coincide.

The meningitic strains of influenza bacilli are closely allied to each other and differ from the ordinary respiratory strains of *B. influenzae*, particularly in their serologic reactions and in their pathogenicity for rabbits.

CONCLUSIONS

Influenzal meningitis appears to be in most instances a primary disease produced by a group of influenza bacilli which are closely allied culturally and serologically.[92]

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92. After the completion of this paper Dr. I. H. Erb furnished information concerning nine cases of influenzal meningitis observed in the Hospital for Sick Children in Toronto in the last two and one-half years. Of the nine patients seven were under 2 years of age. One case occurred in September and three cases in November, 1919; one in November and one in December, 1920; two in November and one in December, 1921. The mortality was 100 per cent. A necropsy was obtained in every instance and the meningitis was considered to have been primary in four of the nine patients, 44 per cent.

STUDIES OF NEPHRITIS IN CHILDREN

I. NEPHROSIS *

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NEW YORK

During the past three years we have had the opportunity of studying about sixty cases of kidney disease in children. According to the clinical findings these cases seem to have fallen into four groups. By means of laboratory data we have endeavored to strengthen this classification so as to make it useful from a diagnostic and therapeutic standpoint:

Group I comprises cases which began either without apparent cause, in children seemingly in perfect health, or in which the mother had, perhaps, noticed that the child was pale. There was little or no elevation of temperature and apparently no accompanying disease. Edema of the face or legs first appeared. It spread rapidly to the remainder of the body. The edema was very persistent, or if it did disappear it showed a decided tendency to recur. There was no hematuria but the urine, at times, was diminished in quantity and always contained large quantities of albumin. The edema was the outstanding feature. The duration of the disease was months or years, and the patient showed no tendency to get well. This malady is known in the earlier literature as nephritis parenchymatosa and has more recently been termed nephrosis by Volhard.[1] Others have used the terms nephropathia epithalialis, nephropathia tubularis and epithelial nephrosis.

Group II comprises cases which began acutely with or without an accompanying acute disease, often with temperature elevation and with or without edema, the edema usually being not extensive, often localized to the face, or to the face and the extremities, and never very persistent. Hematuria was a common symptom. The cases usually lasted a few weeks; occasionally they became subacute and the symptoms would continue a few months, or become chronic and extend for years. Cases of this type are known in the literature as acute nephritis, acute hemorrhagic nephritis or acute glomerulonephritis. When chronic, they are termed chronic glomerulonephritis.

Group III comprises cases observed in private practice for a period of months or years accompanied by an occasional acute stage, but with

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[1] Volhard, F.: Die Doppelseitige Haematogischen Nierenkrankheiten, Berlin, 1918.

none of the outward signs usually seen in kidney disease, such as edema, hematuria or high blood pressure. They are the cases termed by Heubner [2] "paedonephritis."

Group IV comprises cases characterized by marked pallor, headache, vomiting, polyuria, high blood pressure, retinitis, convulsions and death. The entire duration of the disease was about one year. Cases of this description are similar to the contracted kidney, or nephritis with hypertension of the adult.

GROUP I: THE NEPHROSES

The first group to be discussed is the nephroses. These are so named by Volhard [1] and in most of our textbooks they are termed "nephritis parenchymatosa." We use this term strictly in a clinical sense, not having had the opportunity to verify or to classify these cases from a pathologic standpoint. There are seventeen cases in which histories and general course conform more or less to the description given above.

TABLE 1.—Possible Remote Etiologic Factors

Previous History	No. Cases	Years Ago
Scarlet fever	1	7
Measles	2	6
Measles	1	5
Measles	1	4
Measles	1	3
Measles	1	1
Pertussis	1	6
Pneumonia	2	5
Cervical adenitis	1	3
No infectious diseases	4	

TABLE 2.—Recent Possible Etiologic Factor

Case	Disease	No. Cases	When
5	Tonsillitis	1	Six weeks before onset of disease
7	Tuberculosis	1	Many months before and during disease
8	Scarlet fever	1	Four months before onset of disease
11	Diphtheria	1	Four months before onset of disease
14	Otitis	1	Concomitant with onset of disease
16	Scarlet fever (?)	1	Four weeks before onset of disease

Etiology.—In discussing this type of kidney disease and, in fact, in all disease, it is important to examine closely the life history of the patient; for example, a systolic murmur at the apex demands more consideration if one knows there has been a previous chorea.

In Table 1 it will be seen that as a remote etiologic factor only one patient had scarlet fever; five patients had measles, one pertussis, one pneumonia, one adenitis and four had no infectious diseases whatever.

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[2] Heubner, O.: Kinderkrank., Ed. 3 **2**: p. 502.

Although most of these cases did not exhibit an acute condition at the onset of the symptoms, in Table 2 we have tabulated some of the recent acute diseases of these patients. In eleven cases there had been no recent disease so far as we could ascertain, but in five cases some recent disease had preceded this onset.

In analyzing the history of some of these cases, it is interesting to note that one patient (Case 5) had scarlet fever seven years ago. Whether the kidney was damaged at that time and whether the recent tonsillitis was an exciting factor, cannot be determined, for unfortunately we have no accurate interviewing history. Another patient (Case 14) had a recent otitis, otherwise was apparently well but had always had a sallow complexion. A third patient (Case 8) had a questionable scarlet fever four months previously, but was apparently well until swelling of the face was first noted. As is well known, the toxin of scarlet fever usually affects the vascular and not the tubular portion of the kidney which is said to be the lesion in nephrosis. Yet at times, as Heubner[3] has shown pathologically, a tubular nephritis may develop during the course of a scarlet fever infection. Case 16 is a similar one which seemed to develop soon after an attack of a possible scarlet fever, for a sister in the family had scarlet fever at that time. It may, therefore, be possible that the virus of scarlet fever may, at times, give this clinical picture.

As is proven by Volhard's[1] statistics, tuberculosis may be the etiologic factor, for of fifty-five cases of nephrosis cited, fifteen had tuberculosis. Only one of our cases had a possible tubercular etiology. The Pirquet reactions in the remaining cases were negative.

Case 2 is of interest, the patient having had diphtheria a short time previously. In diphtheria, in contrast to scarlet fever, there may be a distinct tubular involvement of the kidney. The diphtheria toxin given intravenously to animals regularly produces an involvement of the kidney tubules, and at the height of the disease albumin and casts appear. Feldman[4] found an involvement of the kidney in 12 per cent. of his cases of diphtheria. Dorner[5] found this type of kidney disease in 6.7 per cent. of his cases. Edema, however, was rarely present, and hematuria and a rise in blood pressure were absent. An interesting clinical fact worth noting is that of Feldman's seventy-three cases of diphtheria complicated by a nephrosis, forty-three patients died, showing the added gravity of this condition in diphtheria. Very few of the cases which recover from diphtheria, however, result in this form of kidney disease.

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3. Heubner, O.: Jahrb. f. Kinderh. **77**:1, 1913.
4. Feldman, H.: Monatschr. f. Kinderh. **19**:491, 1921.
5. Dorner, G.: Quoted by Feldman, Klin. Stud. z. Path. in Behand. der Diphth. Jena, 1918.

Syphilis may cause a symptom complex similar to the one we have studied. Munk[6] describes the clinical picture as one with marked anemia, edema, oliguria, albuminuria, casts and low blood pressure. In our cases the Wassermann reaction was uniformly negative.

Exposure.—Inasmuch as exposure to cold has often been described as an etiologic and exciting cause of kidney disease, it was interesting to see at what time of the year the symptoms in our cases were first noted. It was found that eight cases began in the cold months and nine in the warm months. Although so few cases have been studied, cold or exposure cannot be an important causative factor.

Sex.—Sex seems not to be a predisposing cause. Eight of the patients were females and nine were males.

Age.—Ten of the seventeen patients were of the preschool age giving, perhaps, added evidence of the unimportance of the infectious diseases (Table 3).

There remains, therefore, a considerable number of these cases without any known etiologic factor: the genuine "nephrosis" cases of Volhard. He, as well as Epstein,[7] repeatedly pointed to a general metabolic disturbance, perhaps of the ductless glands, as a cause of this disease, and that these cases do not seem to be primarily a disease of the kidney.

TABLE 3.—Age of Patients

Age, Years	No. Cases
2	1
3-4	5
5	4
6-7	3
8-9	1
10-11	2

Symptoms: *Onset.*—In some of our cases there was a history of pallor or a generally subnormal condition existing for some months previously. In a few cases there was a distinct history of malaise, vomiting and headache; in the majority of cases, however, the first symptom noticed by the parents, was the swelling about the face, the edema increasing with great rapidity. In ten cases the edema began in the face and within twenty-four hours the legs were involved. In other cases the edema of the legs and face occurred simultaneously, and in the course of about a week the other subcutaneous tissues were also involved.

Temperature.—Temperature elevation was not usually present, and the children were not acutely ill; the throat was generally in fairly good condition, only three of the seventeen patients had enlarged tonsils. These children as contrasted with our cases of acute glomerulonephritis were not of the exudative or lymphatic type.

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[6] Funk, F.: Ztschr. f. klin. Med. **78**:1, 1913.

[7] Epstein, A. A.: Am. J. M. Sc. **163**:167, 1922.

Heart.—The heart is usually involved whenever there is general anarsaca, and ordinary physical examination often does not show the true picture. Alwens and Moog,[8] by means of careful roentgen-ray measurements and the rapidly changing heart borders, showed that there is a dilatation of the heart in acute nephritis. Wessler,[9] in like manner, showed that there was distinct hypertrophy in cases of chronic nephritis. So, in our cases, by means of the roentgen ray, it was possible to follow the change in the heart outline according to the presence or absence of general edema. From the pictures it can definitely be stated that there is usually a hydropericardium whenever there is marked general edema.

Chest.—In the pleural cavities, fluid is often present, as demonstrated by the roentgen ray when no signs by ordinary physical examination can be elicited. It is impossible to explain just why the left side of the chest seems more often affected. These cases are often complicated by the infection of the bronchi and the lungs.

Abdomen.—The abdominal cavity, like the pericardium and the pleura, is usually involved but to a much greater extent. Ascites was present at one time or another in all our cases and required paracentesis. The character and analysis of these fluids will be detailed in another portion of the paper.

Edema.—Edema of the subcutaneous tissues was present to a greater or lesser degree at all times. Even when there is no demonstrable edema, there is a marked disposition to it. During marked edema the skin and subcutaneous tissues are greatly distended, and there is a tendency to skin infection, which, however, from our experience, seems not as marked as in the adult, for only once did we see an erysipelas.

Edema of the face and brain: Edema of the face is usually present at one time or another. We believe that edema of the brain may also be present and cause cerebral symptoms erroneously termed uremia. Case 15 had such a symptom complex. The child complained of headache, became semiconscious, cyanotic and would cry out, the attack lasting about twenty minutes and recurring a few times in twenty-four hours. A week later the child was in a semicomatose condition for eighteen hours. During these attacks there was no nitrogen retention of the blood, no increased blood pressure and the eyegrounds were normal.

Abdominal Pain.—This is present at times with a great degree of severity and may be located about the umbilicus. This may be due to an edema of the intestinal wall, but a pneumococcus peritonitis must always suggest itself.

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[8] Alwens and Moog: Deutsch. Arch. f. klin. Med. **133**:364, 1920.

[9] Wessler, H.: Arch. Int. Med. **14**:517 (Nov.) 1914.

Diarrhea.—May occur and is often very severe, this probably being a means of getting rid of the edema fluid. In one of our cases there was a marked diarrhea with mucus and blood, lasting for over two weeks, during which time the ascites and subcutaneous edema disappeared, the child losing 14 pounds in weight.

Anemia.—The anemia in this disease is usually of a mild secondary type, and it is only toward the end of the disease that the hemoglobin may drop below 50 per cent., the red blood cells (Table 4) rarely falling below 3,000,000, there being not much difference in the count before, during or after the disappearance of the anasarca. These children often look very anemic but the absolute degree of anemia is never very great.

TABLE 4.—Blood Count

Case No.	Red Blood Cells	Hemoglobin, per Cent.	White Blood Cells	Polymorphonuclears, per Cent.
1	4,840,000	90	7,200	68
2	....	98	17,000	65
3	5,170 000	80	......	..
	2,150,000	35	22,000	86
4	....	..	......	..
5	4,200,000	78	10,000	60
6	3,900,000	80	7,000	70
7	....	75	9,600	42
8	3,000 000	57	16,000	75
9	4,900,000	85	......	..
10	4,200,000	80	21,000	80
11	4,100,000	80	12,000	55
12	4,400,000	80	10 000	68
13	....	..	......	..
14	3,000 000	65	12,000	50

TABLE 5.—Blood Pressure

Case No.	Age, Years	Blood Pressure		Remarks
		Systolic	Diastolic	
3	6	85	60	
		120	90	Near death
4	..	...	..	
5	11	105	75	
6	5	85	58	
7	10	...	..	
8	4	90	40	
9	8	90	65	
		122	80	
		110	90	No N ret
	AUTHOR: WHAT IS MEANT BY "N ret" ?			
10	5	100	60	
11	3½	105	85	
13	..	...	..	
14	4	95	65	
15	7	120	90	
		125	90	
		135	90	
		130	90	N ret at times
16	2	90	..	
17	7	114	90	

Blood Pressure.—The blood pressure (Table 5) is practically normal. In five cases the systolic pressure rose above 115 and reached 135 in one case. The question of blood pressure in children is always a mooted one, a neurotic temperament, crying and other circumstances may make the blood pressure vary. When the children are doing badly or are near death, as in Case 3, the blood pressure is apt to rise. In Case 15 there was persistently high blood pressure, but only on one occasion was there a high nonprotein nitrogen, later in the disease the nitrogen decreased, yet the systolic blood pressure remained from 125 to 135. Dorner[10] showed that the ingestion of fluid does not cause the blood pressure to rise in cases of nephrosis, for presumably the blood vessels permit water to penetrate into the tissues and no plethora is established. This was confirmed by showing that the total solids of the blood were unchanged. Even intravenous administration of fluid does not cause an increase of the blood pressure. He shows that in addition to increased blood volume there must be a certain contractibility of the blood vessel walls before there can be an increase in blood pressure. In the so-called water test, which will be discussed in detail later, it was observed that the ingestion of large quantities of fluid in a comparatively short time did not increase the blood pressure.

The phenolsulphonephthalein test in these cases showed relatively poor excretion. The test, however, was very unsatisfactory. The dye injected into the edematous tissues is absorbed irregularly and reaches the kidney much more slowly than the two hours alloted to the test, and when given intravenously, the test may also not be accurate because of the permeability of the vessel walls. In one case in which it was given subcutaneously, 25 per cent. of the dye was excreted in two hours with a urine output of 70 c.c.; given intravenously, 32 per cent. was excreted in 100 c.c. of urine. Hessel[11] showed that intravenous injection was, perhaps, a little more satisfactory.

Blood.—The physical character of the blood exhibits a striking quality quite different from the normal, for on drawing blood from the vein and permitting it to coagulate, the serum separates quickly and is distinctly milky, instead of being the normal straw colored, clear serum.

The chemical examination of the blood in the light of the many new microchemical methods which have been devised in the last few years is extremely interesting, examinations being made of the urea, nonprotein nitrogen, uric acid, creatinin, cholesterol, carbon dioxid, sugar, total serum fat and total serum protein and serum chlorids.[12]

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[10] Dorner, G.: Deutsch. Arch. f. klin. Med. **133**:21, 1920.

[11] Hessel, K.: Deutsch. Arch. f. klin. Med. **114**:396, 1914.

[12] *Methods:* Urea—urease (Marshall); nonprotein nitrogen—digestion and titration; uric acid and creatinin with Kuttner's modification of Folin's method; sugar—with Epstein's modification of Benedict's method; cholesterol—Bloor's method; carbon dioxid—Van Slyke's gasometric method; serum chlorids—Van Slyke and Donleary and some by the method of A. S. Wetmore (J. Biol. Chem. **45**:113 [Dec.] 1920); total serum fat—extraction with ether and petrolic ether, using the Roese-Gottlieb method (Rohrig tube); total serum protein—total nitrogen minus nonprotein nitrogen × 6.25.

From Table 6 it will be seen that the urea nitrogen, the nonprotein nitrogen, uric acid and creatinin nitrogen showed very little or no change from the normal, the addition of protein to the food not seeming to affect these values. In changing from a carbohydrate or a karrel diet to a high protein diet very little increase in these values occur. This blood composition, as we will show in a later portion of the article, is one in marked contrast to that seen in cases of acute and chronic nephritis. The nephroses rarely show any retention of nitrogenous substances in the blood, and thus apparently do not terminate in fatal uremia. The coma and convulsions sometimes seen may be due to an acidosis (Case 8) or to an edema of the brain (Case 15).

Case 3 was an exception. In 1915, the child was in Bellevue Hospital, suffering from edema. He was admitted to Mt. Sinai Hospital in 1917 with a history of recurring edema. He was readmitted to Mt. Sinai Hospital in 1919. On this last admission the child was in a moribund and comatose condition. The blood analysis was as follows: urea nitrogen, 114; nonprotein nitrogen, 206; uric acid nitrogen, 6; creatinin, 9; cholesterol, 0.424 per cent., showing an abnormally high nitrogen retention and in addition a great increase in the cholesterol. The fundi were negative. Unfortunately, there were no previous chemical examinations of the blood. But with this marked increase in cholesterol and the history as noted, it is likely that we had a case of nephrosis, the patient dying with the symptoms of uremia.

TABLE 6.—Nitrogenous Elements in the Blood

Case	Urea N	N P N	Uric Acid N	Creatinin N
1	21.4	54.6	1.5	1.5
	14.0	60.0	1.4	1.1
	12.6	39.5		
2	12.6	56.0	1.9	1.5
3	114.0	206.0	6.0	9.2
4	19.6			
	14.0			
5	11.2	37.5	2.5	1.3
	11.2	35.0	3.4	1.8
6	22.4	45.0	3.0	1.3
	14.0	35.5	1.8	1.2
7	21.0	....	...	1.3
	22.4	54.5	1.5	1.7
8	....	87.5	4.0	...
	14.4	41.7	...	2.6
	32.0	63.0	4.4	3.1
	12.6	40.0	4.5	1.5
9	18.2	35.9	1.3	1.1
	15.4	44.4	3.2	2.1
	18.2	45.6	2.8	1.0
	21.6	46.7	2.6	1.5
10	15.4	46.7	1.7	1.2
	14.1	45.5	4.2	1.3
11	16.0	46.9	2.0	1.2
	19.6	53.4	1.6	1.7
	16.8	32.2	2.0	1.3
12	18.2	45.5	1.9	1.2
	18.2	32.2	1.5	1.0
13	12.6	32.9	...	1.2
14	12.2	42.0	1.6	1.2
	25.2	50.0	5.0	1.5
	21.0	49.0	2.8	1.5
	19.6	28.6	1.0	1.0
15	23.8	82.0	3.0	1.0
	12.6	49.5	...	...
	19.6	41.5	1.5	1.4
	14.4	41.0	2.1	1.0
	30.0	56.4	1.8	1.3
	35.2	51.0	1.5	1.2
	12.6	37.0	2.4	1.1
16	18.2	....	1.5	...
	32.2	66.5	2.0	1.6
	47.6	87.6	...	...
	37.8	75.0	...	...
17	11.2	....	...	...

Serum Protein.—The total serum protein of the blood in this condition as shown by Epstein,[13] Volhard[1] and others is almost always reduced, often markedly so. Normally, the serum protein content of the blood after the second year of life is between 7 and 8 per cent. (Utheim [14]) ; in our control cases the protein content in most cases was about 7.3 per cent. It is lowest in the prematurely born and gradually increases up to the second year; it is also low in infants with chronic intestinal disturbance of the so-called athreptic type,[15] and in surgical shock.[16] It is high in conditions in which there is a sudden or continuous fluid loss, such as persistent diarrhea and vomiting, without a sufficient fluid intake, as in intestinal intoxication of infants and in asiatic cholera. In analyzing our cases it will be seen from Table 7 that in only one case did the protein content approach the normal. In all other cases it was low, and in seven it was below 5 per cent.

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[13] Epstein, A. A.: Am. J. M. Sc. **154**:638, 1917 .

TABLE 7.—Total Serum Protein

Case	Date	Urea N	Total Protein, per Cent.	Sodium Chlorid, Mg.	Remarks
1	12/11/21	12.6	6.2	...	After 2 years illness; no edema
4	11/20/21	19.6	4.2	...	Duration 6 months; edema
	12/12/21	14.2	4.35	...	No edema
5	/21	11.2	5.5	...	Duration 4 months; edema
6	7/22/21	14.0	4.96	6.3	Duration 3 weeks; little edema
	12/ 7/21	11.2	5.4	...	No edema
8	4/ 4/21	14.4	5.6	5.6	7 months illness; edema
	4/30/21	32.5	5.3	...	Edema
	11/19/21	40.0	4.3	...	Very slight edema
9	3/ 9/21	18.2	5.6	...	Duration 9 mos.; not much edema
	4/27/21	18.0	4.46	5.6	Edema
10	4/13/21	15.4	4.81	6.0	Duration 1 year; edema
11	4/25/21	16.8	6.3	4.9	Duration 7 months; no edema
	11/25/21	14.0	4.2	...	Slight edema
12	4/ 1/21	18.2	5.9	6.0	History 5 months; edema
14	10/10/21	19.6	4.13	...	Duration 10 months; moderate edema
15	7/21/21	30.8	5.0	6.7	Duration 7 months; moderate edema
16	4/ 9/21	18.2	5.7	5.5	Duration 1 month; edema
	8/24/21	47.6	7.15	...	Edema
17	12/28/21	11.2	4.2	...	Edema

We cannot, however, definitely assert that the diminished serum protein is proportionate to the intensity or the duration of the disease. One of our severest cases (Case 16; the child finally succumbing) had a serum protein content of 7.15 per cent.; on the other hand, one case (Case 11) had a serum protein content of 6.3 per cent. while in the hospital, and seven months later, although the child was in fairly good condition the protein decreased to 4.2 per cent.

Epstein [7] and others have shown that normally the serum albumin fraction of the total serum protein is 65 per cent., and the globulin

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14. Utheim, K.: Am. J. Dis. Child. **20**:366 (Nov.) 1920
15. Marriott, W. McK.: Am. J. Dis. Child. **20**:461 (Dec.) 1920.
16. Smith, H. P.; Belt, A., and Whipple, G. W.: Am. J. Physiol. **52**:72, 1920.

fraction almost 35 per cent. of the total, but that in this type of kidney condition just the reverse is true, the globulin predominates. Unfortunately, we were unable to make these determinations.

The significance of this lowered protein content is difficult to explain, except that it may be one of the factors in the production of the edema. Epstein does not think it is due to the hydremia or migration of serum through the capillary walls. It is true that in some of our cases the plasma volume was altered, the corpuscles in relation to the plasma being reduced in quantity. However, this was not always the case. Nonenbruch,[17] in some experimental work, shows that the change of serum protein does not follow the erythrocyte values. At the end of a saline or gelatin infusion, the protein was lower than could be accounted for by the decrease of the red blood cells. In none of our cases did we find the red cell ration above normal.

Epstein also believes one must take into consideration the tremendous albumin loss in the urine, for these patients pass large amounts of albumin, sometimes for years, even after they are clinically well. We have never seen a case in which the urine was free from albumin, even after three years.

The work of Loeb [18] on the colloidal properties of protein, and that of Palmer, Atchley and R. F. Loeb [19] on the conductivity of salts in the blood when there is a low serum protein may have important bearing on this condition. One must remember, however, that "in vivo" the hydrogen ion concentration and the sodium chlorid content of the blood is constant, the serum protein being the variant in this type of nephritis. These authors suggest a mechanical interference by the protein. Whipple [16] suggests that the protein may exercise a strong stabilizing and protective influence in maintaining a relationship of the circulating blood to the body cells.

Cholesterol and Fat in the Blood.—One of the most striking changes in the chemical composition of the blood in nephrosis is a marked increase in the cholesterol and the fat. This was first pointed out by Chauffard [20] and used by Stepp [21] and Post [22] as an aid in the diagnosis of this form of kidney disease.

Before discussing this phase of the disease, it might be interesting to summarize some of our knowledge concerning cholesterol in the body, and especially in its relation to infants and children. From many examinations of normal children by the methods used in our laboratory

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17. Nonenbruch, W.: Arch. f. Exper. Path. u. Pharmakol. **91**:218, 1921.

18. Loeb, J.: J. Gen. Physiol. **1**:237, 363, 483, 559, 1920.

19. Palmer, W. W.; Atchley, D. W., and Loeb, R. F.: J. Gen. Physiol. **3**: 801, 1921.

20. Chauffard, A., and Grigaut, A.: Ann. de méd. **8**:149, 1920.

21. Stepp, W.: Deutsch. Arch. f. klin. Med. **127**:439, 1918.

22. Post, F.: Deutsch. Arch. f. klin. Med. **128**:61, 1918.

and also according to Beumer,[23] Stern,[24] Bloor[25] and others, the cholesterol content of the blood of young infants and children was found to be approximately the same as that of adults, viz. 0.120 per cent. to 0.220 per cent. The cholesterol in breast milk[26] is very low during the first day of lactation (0.00035 per cent.), then increases rapidly, so that at the end of the first week it is 0.052 per cent., and at the end of the fifth week it again has decreased. This increase in the cholesterol may be of great importance in the new-born period of the child's life. The cholesterol is not found as such in milk but is in the form of an ester.[27] Woman's milk contains 0.139 per cent. and cow's milk 1.26 per cent.; probably a little less than that found in the blood.

The cholesterol content of the various organis of the body has been investigated by Beumer[28] and Chauffard.[20] The suprarenal is the principal depot for cholesterol, containing about 56 gm. of cholesterol per thousand gm. of suprarenal tissue. The liver and kidney contain 2.9 gm. per thousand gm. of the respective tissues, the other organs and tissues containing but a very small amount.

The cholesterol content of the blood is low in all forms of anemia, in moribund conditions, in scarlet fever and in Addison's disease. In rickets, the exudative diathesis, and in cases of edema due to "Mehlnährschaden"[29] it is normal. It is increased in syphilitic aortitis and in some cases of hypertension. Splenectomy[30] causes a distinct rise in the cholesterol content of the blood, and finally the cholesterol content of the blood is markedly increased in the form of nephritis which we are studying.

The metabolism of cholesterol is as yet very little understood. There is according to Blackfan and Gamble[31] a large negative balance in infants, and they believe that cholesterol may be synthetized in the body. The relation of cholesterol to the maintenance of growth does not depend, apparently, on the amount of cholesterol in the food. Wacker and Beck[32] showed that the cholesterol metabolism was dependent on the fat metabolism, and they believe that the cholesterol is carried out with the fat in the stools, thus explaining the negative balance. They showed that the fat partitions in the stools could be altered by giving cholesterol. Chauffard[20] and his co-workers have done a great deal of work in trying to clear up this problem. They attempted to show that the cholesterol metabolism depends on (1) food intake; (2) glands of internal secretion; (3) the liver.

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[23] Beumer, H.: Deutsch. Arch. f. klin. Med. **68**:105, 1920.
[24] Stern, G.: Ztschr. f. Kinderh. **25**:129, 1920.
[25] Bloor, W. R.: J. Biol. Chem. **49**:201, 1921.
[26] Wacker, L., and Beck, K. F.: Ztschr. f. Kinderh. **27**:288, 1921.
[27] Beuner, H.: Monatsch. f. Kinderh. **15**:581, 1919.
[28] Beumer, H.: Monatschr. f. Kinderh. **18**:443, 1920.
[29] Beumer, H.: Monatschr. f. Kinderh. **15**:588, 1920.
[30] Medick, E.: Biochem. Ztschr. **59**:419, 1914.
[31] Blackfan, K. D., and Gamble, J. S.: J. A. M. A. **73**:218 (July 19) 1919.
[32] Wacker, L., and Beck, K. F.: Ztschr. f. Kinderh. **29**:331, 1921.

1. When cholesterol is taken with the food, the cholesterol in the serum increases slightly but returns to a normal level soon after.

2. Of the glands of internal secretion the suprarenal alone is to be considered and seems to be the main depot of the cholesterol, but whether cholesterol is secreted there or only stored in the suprarenal is not known. In unilateral suprarenalectomy, Troissier and Grigant [33] showed that the cholesterol in the blood was high for a few days. Stimulation of the splanchnic plexus to the suprarenal vessels increases the cholesterol output.

3. As for the liver and bile, it has been shown that the cholesterol is excreted in the bile, and, in fact, some think it is the precursor of the bile salts,[34] yet the amount excreted does not approach the total cholesterol destroyed and, perhaps, the liver destroys the remainder (Chauffard).

The intimate association of fat and cholesterol has been pointed out especially by Verse [35] and Bloor.[25] Verse by giving fat alone to rabbits did not produce a lipemia and the animal did poorly, and when he gave cholesterol without fat there was again no lipemia, but the blood cholesterol increased. When he gave cholesterol and fat he produced a lipemia and the animal gained weight. If either one was stopped, the lipemia disappeared. If fat were fed to animals for a time it would take but a little cholesterol to cause a lipemia; but if cholesterol were given alone for a time, it would take a considerable period for the lipemia to develop on giving fat. The blood figures showed better absorption of cholesterol in the presence of fat. The serous cavities in some animals contained fluid, but this fluid had only a very faint trace of cholesterol, but a considerable amount of fat, showing that the fat was more permeable to the capillaries than the cholesterol.

Bloor [25] showed that the normal fat content of the blood is between 0.5 to 0.8 per cent. Milkiness in serum is due to a high fat content, but at times one can get a high fat content without milkiness, as we have seen in some of our cases. After the ingestion of food, he showed there was first an increase of fat in the blood, then of lecithin and finally of cholesterol. The normal lecithin-cholesterol ratio was about 0.96 per cent. Conversely, as the cholesterol was the last to increase in the normal subject so it was also the last to reach its normal level.

The features of a persistent lipemia are: (1) Increase of lecithin and and cholesterol with increase of fat; (2) the greatest increase over

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33. Troissier, J., and Grigaut, A.: Presse méd. **20**:1081, 1912.
34. Wacker, L., and Beck, K. F.: Berl. klin. Wchnschr. **58**:453, 1921.
35. Verse, M.: Beitr. z. Path. Anat. u. z. allg. Path. **63**:789, 1917.

the normal is the fat content; next the cholesterol and finally the lecithin. The origin of the fat in a persistent lipemia is (a) food; (b) the fat deposits in the body.

The origin of the lecithin is from a synthesis of the fat and phosphorus of the body. The origin of the cholesterol is unknown, and the cause of the increase in the cholesterol and why it should accompany an increase of fat and lecithin is as yet unsolved.

TABLE 8.—CHOLESTERIN AND FAT IN BLOOD

Case	Date	Cholesterin, per Cent.	Fat	Remarks
1	10/10/21	0.200	...	Two years after first admission, no edema at present
3	7/15/19	0.424	1.27	Died soon after admission; very edematous on admission
4	11/21/21	0.628	...	Markedly edematous
	12/12/21	0.360	...	Edema gone
	1/13/22	0.242	...	Edema gone
5	9/ 1/21	0.474	...	Very little edema
	9/17/21	0.450	1.2	No edema
	9/24/21	0.552	...	After fat free diet
	11/18/21	0.592	...	Very edematous
6	7/ 4/21	0.776	...	Very edematous
	7/22/21	0.860	1.6	Edema markedly diminished
	12/ 3/21	0.472	...	Six months later no edema
7	5/ 6/21	0.452	...	Slight edema
	6/23/21	0.420	...	Two weeks later no edema
	12/22/21	0.254	0.59	No edema
8	3/12/21	0.314	...	Comatose; blood CO_2 17 (morphin)
	4/ 1/21	0.616	...	Three weeks later, general condition good; nonprotein nitrogen decreased
	4/26/21	0.496	...	Marked diarrhea
	5/11/21	0.418	...	Two weeks later, diarrhea stopped; edema gone
	11/19/21	0.928	...	Six months later, no edema
9	1/24/21	0.412	...	Edema
	3/ 9/21	0.276	...	Edema gone
	4/23/21	0.520	...	Two weeks later, after being home, marked edema
	5/10/21	0.516	...	Marked edema
10	4/12/21	0.464	1.4	Very edematous
	5/28/21	0.352	...	Edema gone
	11/11/21	0.366	...	Edema gone; still in hospital
11	4/12/21	0.592	...	General edema
	3/28/21	0.696	...	General edema
	4/ 6/21	0.424	...	Edema almost gone
	11/15/21	0.376	...	Slight puffiness of face
12	3/31/21	0.284	0.9	Marked edema
	4/13/21	0.170	...	Eleven days after decapsulation, marked edema
	7/19/21	0.334	...	Very edematous
13	10/27/21	0.554	...	General edema
14	5/25/20	0.460	...	General edema
	7/ 6/20	0.648	...	Marked edema
	8/ 4/20	0.430	...	Edema still present
15	3/ 9/19	0.488	...	Edema slight
	4/25/19	0.836	...	No edema
	6/ 1/19	0.738	...	Marked edema
	7/ 1/19	0.532	...	Edema almost gone
	8/11/19	0.616	...	Marked edema; condition poor
	9/20/19	0.464	...	Marked edema
16	5/ 9/21	0.376	...	General edema
	5/13/21	0.532	...	Marked edema; high protein diet begun
	6/25/21	0.388	...	Fourteen days after decapsulation, still edematous
	8/24/21	0.360	...	Still edematous
17	12/28/21	0.740	1.7	General edema

From Table 8 it will be seen that in every one of our cases the cholesterol content of the blood was markedly increased, with the exception of Case 1. This estimation was not made when the patient was originally in the hospital, but only recently when she had been free from edema for some time, so that in this case we cannot make a definite diagnosis of nephrosis from the examination of the blood.

Case 4 is interesting for the child was markedly edematous at the time of the first blood examination. The cholesterol was 0.628 per cent. After losing all his edema, in fact, losing 29 pounds in weight, his cholesterol fell to 0.360 per cent. His serum protein and other nitrogen constituents of the blood were undisturbed. Again, in Case 6, when edema was present, cholesterol was 0.860 per cent., and six months later, without edema, it was 0.472 per cent. It would seem that there is some relationship between the edema and the amount of cholesterol in the blood, yet we have so many determinations to the contrary that this is apparently not the case. Thus, in Case 8, with edema, the cholesterol was 0.616 per cent. The child then had a diarrhea, the edema disappeared and the cholesterol went down to 0.36 per cent. Six months later, however, without marked edema during most of this time, the cholesterol had increased to 0.928 per cent.

Decapsulation of the kidney in two cases seemed to have a temporary effect on the amount of cholesterol in the blood.

In our experience we have found nothing which will directly reduce the amount of cholesterol in the blood for any length of time, be it food, thyroid or surgical procedure.

The total fat content of the blood was naturally high, for the total fat includes the lecithin, cholesterol and fatty acids. The determination of lecithin was impossible at the time because of some technical difficulty. The fat metabolism in the cases in which it was studied was apparently normal, although we did not determine the fat partitions in the stool. Feeding of fat or putting the patient on a fat free diet for a week at a time had no effect upon the cholesterol content of the blood.

Basal Metabolism.—Another interesting fact is the relationship of this hypercholesterolanemia to the suprarenal nad other ductless glands. We realize the interrelationship of these glands and discuss them with great reservation. It has been shown by Epstein and Lande[36] in this Institution that the basal metabolism in these cases is much below the normal (Cases 4 and 5). They took into consideration the artificial increase in body weight in determining the metabolic rate. As these patients improve, the basal metabolism approaches nearer to the normal. Furthermore, the successful therapeutic use of thyroid by Eppinger,[37] Epstein[7] and in some of our cases would point to a probable endocrine relationship. Epstein believes that the metabolism is always low when the cholesterol is high, and high when the cholesterol is reduced in

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36. Epstein, A. A., and Lande, H.: (Personal communication).
37. Eppinger, H.: Pathologie u. Therapie des Menschlichen Odem., 1917.

amount. Aub, Forman and Bright [38] show that after suprarenalectomy in the cat the basal metabolism was low, but they gave no cholesterol figures.

THE CAUSE OF EDEMA IN NEPHROSIS

The cause of the edema has been the subject of investigation for many years. Many theories have been advanced to explain it. To the kidney, naturally, was ascribed the edema, for one observed so frequently oliguria with edema, and diuresis with the disappearance of the edema. All observers, however, now agree that the kidney is probably the least offending link in the chain of causes. This chain may tentatively be made up of (*a*) physical, biological or chemical change in the blood itself; (*b*) change in the walls of the capillaries; (*c*) change in the physical or chemical composition of the tissue fluids; (*d*) change in the walls of the venules or lymph channels; (*e*) change in the body cells themselves; (*f*) disturbance of the endocrine gland; (*g*) abnormal nervous control; (*h*) pathologic lesions of the kidney.

A discussion of each of these subjects would take us too far afield, and one may be so linked with the others that it is almost impossible to discuss them separately. Yet some of the newer work might be of interest.

The chemical composition of the blood is so changed that it is very tempting to lay the blame here. As shown before, the serum protein content is consistently diminished, yet this is not the case when edema occurs from some other cause. This decrease in blood protein is not necessarily due to a change in the blood volume and the presence of a hydremia. This was well illustrated in Case 4. The serum protein content was 4.2 per cent. during general anarsaca. Within a week, a marked diuresis having taken place, the child lost 29 pounds in weight and all manifest edema had disappeared, yet the blood protein remained the same. It would not appear, therefore, that the reduction in the protein content of the blood is a great factor.

The sodium chlorid content of the blood did not vary much, never going above 6.1 mg. or below 5.1 mg. per 100 c.c. of blood, independent of the presence or absence of edema. These figures were obtained on a fasting stomach. Atchley [39] showed that there may be no change in the sodium chlorid content of the blood plasma, independent of intake or urinary excretion and, paradoxical as it may seem, to the apparent chlorid balance.

Oehm [40] has recently reported some interesting experiments in relation to the control of diuresis by means of the physical and chemical composition of the blood. He uses two sets of animals—one fed on a dry diet, and the other on a moist diet. During the experiment he repeatedly determined hemoglobin, the serum protein and the sodium chlorid. In both sets of animals the water from the blood goes into the tissue and carries along with it the protein. In the dry fed animals more water remained in the blood than in the moist fed animals, so that the blood was just as rapidly diluted. There is no hydremia in the case of moist fed animals to account for the diuresis which occurs. In tying off the kidneys in both sets of animals there is no difference in the chemical composition of the blood.

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[38] 38. Aug. J. C.; Forman, J., and Bright, E. M.: Am. J. Physiol. (Proc.) **58**:293, 1921.

[39] 39. Atchley, D. W.: Arch. Int. Med. **22**:370 (Sept.) 1918.

[40] 40. Oehm, C.: Verhandl. des Congress f. inn. Med., 1920, p. 137.

The high cholesterol content of the blood does not seem to have any relation to the transudation of fluid and the causation of edema, for, as we will show, there is little or no cholesterol permitted to go through the walls of the capillaries into the edema fluid. It is well known that there is a constant interchange of water, organic and inorganic substances, from the blood into the tissue spaces, thence to the cells and back to the tissue spaces. MacCallum[41] showed that there was no direct connection between the lymph spaces and the tissue spaces and that the lymph channels ended in a blind pouch.

It is important, therefore, to differentiate between (*a*) transudate, (*b*) tissue fluids and (*c*) lymph fluids.

(*a*) Transudate is that fluid which goes through the walls of the capillaries. It may be normal or pathologic.

(*b*) Tissue fluids are that part of a transudate taken up by the cells and given off by the cells.

(*c*) Lymph is that fluid which flows out of the lymph channels. Fluids and other substances from the blood must pass through these tissue spaces before going to all the organs and returning to the blood.

After hemorrhage there is a marked flow of tissue fluid into the blood. This is not from the lymph for there is no demonstrable increase of lymph flow from the lymphatics. Conversely, after transfusion there is a flow of fluid towards the tissues.

Magnus[42] found that 19 per cent. of fluid given intravenously had left the blood stream in three minutes and 50 per cent. had left it in twenty minutes. The injection of hypotonic salt solution causes an exodus of water into the tissues, and salt into the blood. The composition of the blood remains fairly constant. It seems to be the function of the walls of the capillaries to permit the exit or entrance of fluid and other substances into the blood stream, whenever the balance between blood and tissues is disturbed.

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[41] MacCallum, W. G.: Text Book of Pathology, 1916, p. 41.

[42] Magnus, R.: Arch. f. exper. Path. u. Pharmakol. **42**:250, 1899; **44**:68, 1900.

Hooker,[43] and more recently, Wallace and Pellini,[44] have demonstrated specific capillary poisons which permit of great permeability and this way be the cause of graver general disturbances in the body. Some of these poisons have a selective action on capillaries of certain parts of the body as those of the liver. It is tempting to consider the cause of the disease we are describing as due to a capillary poison acting especially on the skin, muscle and perhaps kidney capillaries.

From the physicochemical standpoint Priestley[45] thinks that the interchange of fluids may be due to a diminution in the electrical conductivity of the plasma, and a difference in what he calls the diffuse pressure. He has likened the blood to a gas, and has tried to explain the diffusion of fluids out of and into the blood stream by the same laws as govern gases. He defines the diffusion pressure of water on both sides of the membrane, as proportioned to the water molecules and the total molecules.

An analysis of the tissue fluids themselves might help to clear up the problem (Table 9). Unfortunately, it is impossible to obtain fluid from the interstices of the tissues in the normal person. In various forms of edema, however, it is shown that these tissue fluids differ. Beckman,[46] who has examined a great variety of edema fluids, has shown that the edema fluids in the nephrosis cases contain only 0.1 per cent. protein. In our cases it was never higher than 0.18 per cent. In the cardiac, the protein content was 0.4 per cent. and in the nephritic the protein content was often over 1 per cent. It will be seen, therefore, that in edema from various causes the vessel walls will differ as to their permeability to protein. Whether 0.1 per cent. protein, as occurs in nephrosis, is greater than the normal cannot be stated. It is this permeability of the vessel wall to protein that Eppinger[37] called the albuminuria of the tissues and is a feature of all edema fluids.

The sodium chlorid content of the various edema fluids is about the same, 0.6 per cent. Thannhauser[47] gave sodium chlorid to nephritics and found that the sodium chlorid of the edema fluid and the blood increased, but the latter, however, to a lesser extent. Soon, however, the sodium chlorid of the blood and edema fluid diminished rapidly, but there was no increase of the salt in the urine. Beckman[46] believes that there is another depot for the salts which is probably the tissue cells.

The cholesterol content of the edema fluids is practically nil. Apparently, the capillary wall is impermeable to this substance.

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43. Hooker, D. R.: Physiol. Rev. **1**:112, 1921.
44. Wallace, G. B., and Pellini, E. J.: Arch. Int. Med. **28**:711 (Dec.) 1921
45. Priestly, G. J.: J. Physiol. **55**:306, 1921.
46. Beckman, K.: Deutsch. Arch. f. klin. Med. **135**:39, 1921.
47. Thannhauser, S. J.: Ztschr. f. klin. Med. **89**:181, 1920.

The relation of the endocrine glands to edema has been emphasized by Eppinger in his monograph. Thevenat [48] was the first to use thyroid as a diuretic. Soon afterward Eppinger began his studies of thyroid extract as an effective diuretic in edema and especially in the so-called nephrotic edema. The manner in which it works is not definitely known. He concluded that it had no specific action on the kidney. He has proven that water and salt are excreted more rapidly after the administration of thyroid. Under normal conditions salt given subcutaneously is excreted more rapidly than if given by mouth. In some abnormal conditions, especially in nephrosis, salt given subcutaneously is excreted less rapidly than that given by mouth. If thyroid is administered the patient will have an excretion which is normal or above normal. Hence, Eppinger believes that there is certainly no selective action on the kidney. Epstein [36] believes that the thyroid increases the basal metabolism. The specific dynamic action of the protein is raised and the colloidal combination of protein in the tissue fluids is changed, thus perhaps setting free the water in the tissues. The hypophysis, on the other hand, has a direct action on the kidney (Oehm [40]).

TABLE 9.—ANALYSIS OF EDEMA FLUIDS

Case No.	Diagnosis	Specific Gravity	Protein	Sodium Chlorid	Cholesterin	Fat
13	Nephrosis	1.0059	.....	0.64	0.212	....
5	Nephrosis	1.010	0.187	0.65	None	0.03
4	Nephrosis	1.010	.....	....	None	....
16	Nephrosis	.....	.....	....	Trace	....
	Cardiac	1.010	0.412	0.66	.....	....

Analysis of Edema Fluids (Beckman [46])

Diagnosis	Protein	Sugar
Nephrosis	0.1	0.123
Nephritics	1.0	0.116
Cardiac	0.4	0.127
Cachexia	0.2	.....

Ascitic Fluids

14	Urea N per 100 c.c.	19.6	36
	N. P. N. per 100 c.c.	28.6	70
	Uric acid per 100 c.c.	1.5	
	Creatinin per 100 c.c.	1.0	

(Cardiac)	Total N	0.256	Protein	1.69	Sp. Gr.	1.015
	Cholesterin	0.020				
	NaCl	0.62				
	Bile plus					

Oehm has shown that there is a substance in the duodenal mucosa that has a diuretic action. He also thinks that products of metabolism simultaneously stimulate the tissues and the kidney.

That the central nervous system may have some control of the water excretion is shown in some of the intracranial diseases, notably in the disturbance of the hypophysis or tumors of the posterior fossa. The experimental work of Veil[49] and Leschkes,[50] demonstrated that injury to the brain in the region of the fourth ventricle causes a polyuria with a hyperchlorinemia, whereas an injury to the midbrain produced polyuria but no hyperchlorinemia.

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[48] Thevenat, L.: Progrès. méd., 1913, p. 237.

It has been known for a long time that section of the renal nerve to one kidney causes an increased flow of urine on that side. This is probably due to a circulatory disturbance in the kidney. E. K. Marshall and A. C. Koll[51] have confirmed this observation, but have also shown that identical results can be obtained by section of one splantic nerve to the suprarenal or removing one of the suprarenal glands.

From the foregoing it will be seen how complex is the problem of fluid excretion.

WATER TEST

In considering the many important and interesting facts already cited, and realizing the importance of the extra renal element, it must not be forgotten that the excretion of water by the kidney gives some very valuable information after all. Many functional kidney tests have been described, such as the excretion of dye stuffs, or salt, of urea and of water. We cannot go into a discussion as to the value of all these tests.

In the course of our work it appeared to us that the excretion of water alone or water with the addition of salt gave considerable information. The test could be carried out very easily and done at home without any difficulty. However, we were very careful with the salt in our nephrosis cases, so that we finally confined ourselves to the administration of water alone. For a long time it has been known that water ingested by a normal person is excreted in a fairly regular manner. This fact was first made use of by Koryani,[52] later amplified by Strauss[53] and finally modified by Volhard.[1] The test for adults is described by Volhard as follows:

> After the usual evening meal the patient is kept in bed for the following one and a half days. At 8 a. m. the patient empties the bladder and this urine is discarded. Immediately after, an adult is given 1½ liters of ordinary water which is swallowed as quickly as possible. No breakfast is given. The patient is asked to urinate every half hour for the next four hours. These specimens are kept separately for further examination. At the end of the four hours, a dry meal is given, such as meat, thick cereal and bread. But no additional fluid of any kind is permitted until the next morning at 8 o'clock. At 6 p. m. another such fluid free meal is permitted. After the first four hours (from 8:30 a. m. to 12:30 p. m.) the patient urinates whenever desired, keeping each specimen separately, the final specimen being collected at 8 a. m., which completes a twenty-four hour cycle. This specimen is preserved. The specimens are examined as to volume and specific gravity.

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[49] Veil, W. H.: Verhandl. d. Congr. f. inn. Med. **32**:134, 1920.

[50] Leschkes, E.: Ztschr. f. klin. Med. **87**:201, 1919.

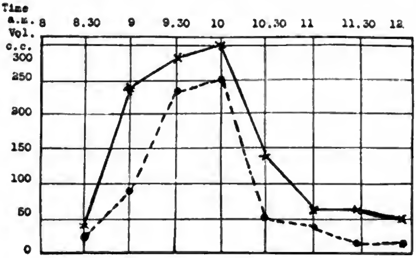
[51] Marshall, E. K., and Koll, A. C.: Am. J. Physiol. **49**:302, 1919.

[52] Von Koryani, A.: Physic. Chem. u. Medizin. **2**:133, 1908.

[53] Strauss, H.: Chronische Nierenentzündung, Berlin, 1902

It will be seen from the chart that in the normal cases almost the entire fluid ingested will be excreted within the first four hours. The first specimen voided is small in amount, then the volume increases rapidly until the end of the fourth specimen when it begins to drop to a relatively low figure. The specific gravity follows the volumetric change very closely, the urine becoming more and more diluted, the specific gravity often being as low as 1.001 at the end of the third specimen, then it gradually increases so that the specific gravity in the last specimen may be between 1.030 and 1.040.

Of course, in children the amount of water given must be considered. Aschenheim,[54] Stransky and Belant [55] have investigated the use of this test in infants, and Ohlman [56] in older children. We have appended a chart taken from Ohlman [56] which is, however, in the form of percentage intake excreted in twenty-four hours.



Results of water test; intake, 900 c.c. Amount excreted every thirty minutes for the first four hours. X———X, normal; ● — — — — ●, case of nephrosis.

The amount of water excreted depends on the age of the child; the younger the child the more water is retained. In a general way it may be said that a normal patient should excrete about the amount ingested at the end of four hours. Of course, this excretion depends somewhat on atmospheric temperature and the activity of the person. The fluid lost by respiration is fairly constant. The addition of salt to the water has a marked effect. The diuresis sets in a little sooner but the total quantity excreted is considerably lower. One other fact must be considered during this test. A person who has been on a dry diet, or a diet comparatively poor in water, will have a much diminished excretion as compared with one who has been on a normal amount of water previous to the inauguration of the test. It is important, therefore, to have the amount of fluid to be ingested on the test day about equal to the amount usually taken by the patient.

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[54] Aschenheim, E.: Ztschr. f. Kinderh. **24**:281, 1920.

[55] Stransky, E., and Balint, A.: Jahrb. f. Kinderh. **93**:350, 1920.

[56] Ohlman, J.: Ztschr. f. Kinderh. **26**:296, 1920.

We must bear in mind from the work of Priestley [45] that the kidney has optimum excretory power per certain unit of time.[57] He gave larger amounts of water to normal persons hour after hour and found that the kidney would not or could not excrete more than a certain amount in a given period of time. Priestley does not believe that there is any great relation between the water and the salt excretion. After drinking 2 liters of water there is a transitory increase in the absolute amount of chlorid excreted per hour. This washing out, however, lasts only a very short time and a normal chlorid excretion is resumed even though diuresis is increasing.

TABLE 10.—NORMAL WATER TEST—940 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	40	1.010
9:00 a.m.	240	1.004
9:30 a.m.	290	1.008
10:00 a.m.	300	1.008
10:30 a.m.	140	1.008
11:00 a.m.	60	1.010
11:30 a.m.	60	1.012
12:00 m.	50	1.014
Total	1,180	
8:30 p.m.	430	1.030
8:00 a.m.	140	1.040
Full total	1,750	

TABLE 11.—WATER TEST IN NORMAL CHILDREN (FROM OHLMAN) [56]

Age	Water Intake, C.c.	Excretion in 5 Hours, %	Excretion in 5 Hours if 0.7 per Cent. Salt is Added, %
First 6 months	100	60 to 80	27 to 43
Second 6 months	200	80 to 90	49 to 70
1 to 4 years	300	91	70
4 to 6 years	400	133	87
6 to 10 years	600	175	107

This water test was used in nine of the reported cases; sometimes only once, other times more frequently. We were careful not to use this test during a period of diminishing edema and only when the condition of the child had been fairly constant for a few days. In judging the amount of water to be given we considered the age of the patient and the amount of urine he was excreting for a few days previously, although always bearing in mind the fact that during the previous days the fluid had not been given all at one time but distributed throughout the day and that food was also given at various times of the day. These facts undoubtedly affect the water excretion.

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[57] Priestley, J. G., and Haldane, J. S.: J. Physiol. **50**:296, 1916.

RESULTS OF WATER TEST

Case 1.—A child, aged 11 (Case 5), had very little edema at the time the test was made. Weight, 70 pounds.

The excretion increased rapidly for the first one and one-half hours and then receded rapidly. He did not excrete the entire 1,000 c.c. during the first four hours but did at the end of the twenty-four hours. This retardation we have found to occur frequently in these cases of nephrosis.

A second test, made two and one-half months later, when he was very edematous (weight, 95 pounds), showed much the same characteristics. His diuretic curve was normal. He excreted 500 c.c. of the total in the first four hours, 100 c.c. more than the intake in the twenty-four hours. Only 2 gm. sodium chlorid was excreted during the entire day.

Case 2.—A child, aged 7 years (Case 4), very edematous, weight being about the same two days before and after the test. On an intake of 500 c.c. he only excreted 250 c.c. Given a water test of 500 c.c. a marked diuretic effect was seen. Why in some instances the ingestion of large quantities of water causes a diuresis at one time and not at others cannot be explained.

TABLE 12.—Water Test: Case 1 (5), 1,000 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	50	1.006
9:30 a.m.	150	1.002
10:00 a.m.	200	1.001
10:30 a.m.	200	1.001
11:30 a.m.	25	1.004
12:00 m.	50	1.008
Total	695	
6:00 p.m.	130	1.022
9:00 p.m.	70	1.022
8:00 a.m.	220	1.022

TABLE 13.—Water Tests Case 2 (4), 500 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	145	1.024
9:00 a.m.	30	1.004
9:30 a.m.	80	1.008
10:00 a.m.	13	1.006
10:30 a.m.	10	1.010
11:00 a.m.	10	1.012
12:00 m.	10	1.020

Case 3.—A child, aged 10 years (Case 7), excreted from 300 to 400 c.c. in twenty-four hours for previous few days. It was given 600 c.c. in the water test.

Table 14 shows a normal character to the excretion but a diminished output—357 c.c. of the 600 c.c. excreted in the first four hours; 500 c.c. in twenty-four hours.

Case 4.—Child aged 4 years (Case 8), with moderate edema. Although the total excretion is good the specific gravity never went above 1.018.

Case 5.—Child, aged 5½ years (Case 11), with moderate edema. The first water test was followed by a marked diuresis. One month later, the boy, being in about the same condition, was given 500 c.c. but only excreted 250 c.c. in the first four hours and 326 c.c. in the twenty-four hours. We are unable to explain this difference. The concentration in both specimens was normal.

Case 6.—A child, aged 5 years (Case 14), had been edematous for a long time, the weight changing but little. From Table 16 it will be seen that the excretory curve is a little different from that of other cases. The diuresis continued for a longer period and no single specimen contained more than 100 c.c. Either the water was not brought to the kidney to be excreted, or the kidney did not have the power to eliminate the fluid.

In conclusion, it is quite evident that the manner in which the water is excreted in this type of case in most instances approaches very close to the normal. At times the total quantity excreted is not quite up to the normal. It seems remarkable that an individual with such marked edema should, when given large quantities of water, excrete most of it in a short time; very little is retained, showing well that the excretory power of the kidney is not diminished. Either this water goes directly into the tissues and other fluid is brought to the kidney, or this water goes directly to the kidney, the tissues being so saturated that they do not take up any more fluid.

TABLE 14.—Water Test: Case 3 (7), 600 C.c.

Time	Volume, C.c.	Specific Gravity
9:00 a.m.	125	1.004
10:00 a.m.	162	1.001
11:00 a.m.	20	1.004
12:00 m.	50	1.007
Total	357	
1:00 p.m.	20	1.010
5:00 p.m.	46	1.024
8:00 p.m.	22	1.028
5:30 a.m.	31	1.024
8:00 a.m.	19	1.024

TABLE 15.—Water Test: Case 4 (8), 800 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	57	1.010
9:00 a.m.	145	1.012
9:30 a.m.	153	1.002
10:00 a.m.	165	1.002
10:30 a.m.	130	1.002
11:00 a.m.	45	1.002
11:30 a.m.	27	1.010
12:00 m.	27	1.006
Total	749	
5:00 p.m.	45	1.016
4:00 a.m.	105	1.018
8:00 a.m.	40	1.014

TABLE 16.—Water Test: Case 6 (14), 600 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a.m.	60	1.002
9:00 a.m.	50	1.002
9:30 a.m.	100	1.002
10:00 a.m.	50	1.002
10:30 a.m.	100	1.002
11:00 a.m.	60	1.004
11:30 a.m.	50	1.006
12:00 m.	20	1.004
Total	490	
8:00 a.m.	20	1.012

Urine.—The ordinary chemical and microscopic examination of the urine in this class of case is so well known that one need not go into detail; the usual high specific gravity and the intense albuminuria with comparatively few casts is the common feature. Red blood cells are occasionally found. Even with a concomitant acute infection, hematuria is not usually present. Funk was the first to find double refractory bodies in the urine. Gluck found these lipoid bodies to be present after giving cholesterin.

Nitrogen excretion is normal. Using a modified Mosenthal diet, in no case was there ever a real nitrogen retention. Sodium chlorid excretion, however, was affected. The sodium chlorid excretion in the urine was almost nil during the edematous stage. During diuresis as much as 25 gm. sodium chlorid was excreted in twenty-four hours. In this latter case the concentration of the sodium chlorid was 0.6 per cent. in a volume of 4,000 c.c.

Complications.—The complications seen in this disease are all due to the diminished immunity which these patients seemed to have for the acute infection. Those involving the skin, such as erysipelas, seem to be less frequent than similar cases in the adult. One patient died of a complicating diphtheria. Although discovered early, and large doses of antitoxin being given, the membrane spread with remarkable rapidity.

TABLE 17.—Duration and Prognosis

Case No.	First Seen	Last Seen	Duration	Condition When Last Seen
1	August, 1919	December, 1921	2 yrs. 3 mos.	Albumin ++; no edema; general condition good
2	February, 1919	May, 1919	5 months	Dead; pneumonia
3	1915	July, 1919	4 years	Dead; uremia (?)
4	September, 1921	Jan. 16, 1921	4 months	Condition good; no edema
5	September, 1921	Jan. 14, 1922	4 months	Dead; pneumococ. peritonitis
6	July, 1921	December, 1921	6 months	Urine, albumin ++; no edema
7	January, 1921	January, 1922	1 year	Urine, albumin ++; no edema
8	July, 1920	December, 1921	1½ years	Urine, albumin ++; slight edema
9	July, 1920	December, 1921	1½ years	Urine, albumin ++; no edema; in hospital
10	April, 1920	December, 1921	1¾ years	Urine, albumin ++; slight edema; in hospital
11	August, 1920	December, 1921	17 months	Urine, albumin +; slight edema; cholesterin 0.376%
12	June, 1920	December, 1921	18 months	Albumin ++; slight edema; in hospital
13	October, 1921	December, 1921	2 months	Very marked edema
14	March, 1920	January, 1921	10 months	Dead; diphtheria
15	January, 1919	July, 1921	½ year	Dead; pneumonia (?)
16	March, 1921	November, 1921	8 months	Dead; nephrosis
17	November, 1921	January, 1922	2 months	Dead; pneumococ. peritonitis

Pneumococcus infection seems especially virulent in every case. When the patient complains of abdominal pain one would always have in mind a pneumococcus peritonitis. Two of our patients (Cases 5 and 17) died of this complication. Two died of pneumonia. True uremia, in the sense of a stupor associated with an increasing nitrogen retention, is rarely seen. When coma supervenes it is not associated with a nitrogen retention and is usually of short duration. It may best be thought of as a temporary cerebral edema.

Prognosis.—From our experience the prognosis of these cases as to life is bad. Six of the seventeen patients died, and none of the others can be declared well, although some have been observed for more than three years. Of the fatal cases, the duration of one case was two months and another four years. This latter case had a fairly constant edema. Death usually occurs from some intercurrent infection, although one child seemed to die of uremia. Table 17 gives a good idea of the present status of our cases. We hope to give a more detailed picture of the prognosis at some future date. We are continuing our observations on ten of the cases here reported.

Treatment.—In a condition such as this with its chronicity and marked periods of apparent improvement occurring without any definite cause, one must be very cautious in ascribing great value to any one special procedure. In the present state of our knowledge, prevention can hardly be considered. We feel sure that tonsillectomy and the removal of other foci play but a small rôle in the care of these children, except, perhaps, to put them in the best possible condition. As stated before, these children are not usually of the lymphatic type.

The treatment of the disease must necessarily be directed to (*a*) the albuminuria; (*b*) the pathologic changes in the blood, and (*c*) the edema and the oliguria. From our observations we can say that we have been unsuccessful in permanently affecting the albuminuria or the cholesterinemia. Although at times the albuminuria would be less, at other times, while on the same method of treatment, there would be a marked increase in the albuminuria. The casts in the urine would be present or absent for weeks at a time, without any indication of a real benefit to the patients or foretelling a relapse of the symptoms (edema). The high cholesterin in the blood seemed never permanently affected by whatever method of treatment, and at times when all, or nearly all, manifest edema had disappeared the cholesterin values were highest.

There remains, then, the treatment of the edema and, coincidentally, of the oliguria. This has for years been attacked by means of diet, drugs or both. In addition operative procedures have also been employed. The elimination of fluids from the body is the prime object and the many theories by which this may possibly be accomplished have been treated of in previous portions of this article. Practically, we may consider first the restriction of water in the diet. We have tried this in many cases and systematically have given about the amount eliminated by the kidney for a few days previously, or even reduced the amount to a very small fraction of the kidney excretion but have found that this does not cause an elimination of the body fluids and the edema remains. In fact, we have found that the ingestion of large amounts of water within a short period of time, as in the water test, has a marked diuretic effect and the regular administration of this diuretic water shock has been suggested by Dorner[58] and used in some of our cases. At the present writing, it is our opinion that almost the normal amount of water according to age can be given to these cases without any harm. The Karrel treatment has been tried and the amount of milk given was considerably less than the amount of fluid according to the age. In some cases this would cause a dimunition of the edema, while in others it had absolutely no effect. Indeed, in the same case it would be effectual at one time, and ineffectual at another. Epstein[59] seems to think that these are different types of the disease, yet when this occurs in the same case, there must be another explanation. It seemed to us that whenever the small amount of salt present in the milk was really an overdose, the edema was unaffected. In regard to other articles of food in these cases, there have been many conflicting opinions. From our observation we can definitely say that only one constituent of diet seems to do harm, and that is the salt. We have seen considerable carbohydrate given, without much effect upon the edema and no change in the chemical composition of the blood. This is also the case with fat and protein.

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[58] Dorner, G.: Med. Klin. **17**:45, 1921.

The administration of protein, in whatever form, has no deleterious effect on the general condition, the edema or the chemical composition of the blood. This brings us to a discussion of excessive amounts of protein in the diet as recommended by Epstein.[7] There can be no doubt that his high protein diet does good in many cases, and it has seemed to us especially in those cases where the patient has been on a very low protein diet previously. It would appear that this is another example of treating the child as a whole; not letting his general condition deteriorate by a very onesided diet, especially in so important a principle as protein. Epstein's explanation of the edema being due to a dimunition of a blood protein caused by excretion of albumin in the urine does not seem to be proven, for in the first place it has been shown by Nonnenbruch[17] that the serum protein of the blood has little to do with the egress of water from the capillaries into the tissues. In the second place, in some of our cases in which we have given large amounts of protein over periods of months, the edema may or may not have disappeared, yet the serum protein of the blood still remains low. The relationship of globulin to the albumin in the blood serum, to which Epstein has drawn attention, we cannot discuss for we have no experience in observing this. As far as our experience with diet in this disease is concerned, it seems that it is best combated by placing the child on a fairly adequate amount of water, an absolutely salt free but normally balanced diet as far as the remainder of the food principles is concerned. Whether it is necessary to give added amounts of protein to make up for the loss in the urine we cannot definitely say for we are studying this phase of the disease. That large amounts of protein in the food tend to raise the protein in the blood does not seem to be the case.

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[59] Personal communication.

As far as the treatment of the edema by means of the ordinary diuretics is concerned it can be fairly definitely stated that they are of no avail, and the saline diuretics may be of decided harm. We have used theocin for its supposed direct action on the kidney and have had no beneficial results. The use of thyroid, however, seems to raise the basal metabolism in these cases and in many instances has a miraculous effect on the edema. We have taken the suggestion of Epstein and Lande,[36] have begun with small doses of thyroid and controlled the increase by basal metabolism observations.

Decapsulation was tried in two of our cases with very little or no effect on the edema, the blood chemistry or the general condition. We are aware that in the literature there are a sufficient number of cases published to warrant this procedure, although in our series the result has been nil.

To sum up, then, our treatment of these patients is to keep them in bed while they have any manifest edema, place them in the best hygienic surroundings, on an absolutely salt free diet, with a normal amount of fat and carbohydrate and an amount of protein somewhat in excess of the normal; a fluid intake almost that of the normal. If this does not suffice, we have added thyroid extract in increasing amounts. As far as the cure of the disease is concerned, the reduction of the albumin in the urine, the cholesterin and fat in the blood, this we have been unable to accomplish.

REPORT OF CASES *

CASE 5 (Hospital No. 213050).—Male, aged 11, admitted Sept. 1, 1921. The child had had recurrent edema of about three months' duration, apparently caused by nasopharyngeal infection, but never any hematuria. However, a history of scarlet fever some years previously might point to the nasopharyngeal infection as a cause for a relighting of an old infection of the kidneys, although there were no symptoms in the interim, as far as the history can elucidate. From the chemical examination of the blood for a period of two months, the low blood pressure, high cholesterin, and the recurrent edema, it would seem that this is a case of nephrosis. Thyroid was given beginning with ¾ grain three times a day, gradually increased to 3 grains three times a day. During this time the edema remained about the same and the basal metabolism had not been accelerated, remaining between —20 and —30 per cent. The child did not respond to treatment, although at one time or other on a salt-free diet, a fat-free diet and, for the past two months, on a high protein diet. Whether this condition was of only a few months standing or whether it dated from the scarlet fever, seven years ago, is impossible to state definitely. The child died of lobar pneumonia.

Family History.—Negative.

Previous History.—Measles (time unknown); scarlet fever seven years ago, but no evidence of kidney disease at that time.

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* These cases have been selected as illustrating special points made in the text. All the cases studied will appear in the reprints.

Present History.—Just before the present illness, the child had difficulty in swallowing and was told that he had tonsillitis. A week later (six weeks ago) his mother noticed that he had swelling of arms and legs. After three weeks the swelling disappeared entirely. Was out of bed one week when the edema reappeared. He had no nocturia, hematuria or polyuria. His appetite was good and he had no fever.

Physical Examination.—The child was well developed, fairly well nourished. Face: edematous; some enlargement of cervical lymph glands. Heart: apex beat in fifth space and nipple line; second aortic sound exceeds that of the second pulmonic in intensity; faint systolic murmur at apex. Abdomen: shifting dulness. Extremities: some edema of feet.

Laboratory Examination.—Sept. 1, 1921: Hemoglobin, 78 per cent.; erythrocytes, 2,420,000; leukocytes, 10,000; polymorphonuclears, 68 per cent.

Pirquet and Wassermann Tests: negative.

Urine: acid; specific gravity, 1.020; albumin, trace; many hyaline and granular casts.

Blood Pressure: 105/75.

Blood Chemistry: Urea nitrogen, 11.2; nonprotein nitrogen, 37.5; uric acid, 2.5; creatinin, 1.3; cholesterin, 0.474.

The excretion in four hours is fairly good. The amount of the twenty-four hour period is above that of the intake. The concentration is good.

TABLE 21.—URINARY EXCRETION IN CASE 5

September 5: Water Test, 1,000 c.c.

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	50	1.006
9:30 a. m.	150	1.002
10:00 a. m.	200	1.001
10:30 a. m.	200	1.001
11:30 a. m.	25	1.004
12:00 m.	50	1.008
Total	695	
6:30 p. m.	130	1.022
9:00 p. m.	70	1.022
8:00 a. m.	220	1.022

September 6: Intake, 625 c.c.; excretion, 460 c.c. Weight, 82 pounds and 9 ounces. Fundi, negative.

September 7: On a salt-free diet; fluid limited to 800 c.c.

September 9: Temperature suddenly went up to 104 F.; came down to normal next day, without any apparent cause.

September 12: Edema is very much diminished and the weight has dropped to 78 pounds. Child has been vomiting all day; continued vomiting for two or three days. All food has been excluded and Delafield's mixture given.

September 15: Intake, 700 c.c.; excretion, 600 c.c. Weight, 77 pounds and 14 ounces.

September 17: Thick cereal, eggs and toast added to diet.

Blood Chemistry: Urea nitrogen, 11.2; nonprotein nitrogen, 35; uric acid, 3.4; creatinin, 1.8; cholesterin, 0.450 per cent.

For one week child was put on a fat-free diet and the cholesterin again estimated; the results showed no diminution, rather an increase in the cholesterin of the blood. Cholesterin, 0.592 per cent.

Basal Metabolism: —20 per cent. below normal. Fat in blood serum, 1.2 per cent.

September 28: Blood pressure, 90/70. Patient is out of bed.

October 1: Intake, 700 c.c.; excretion, 650 c.c. Weight, 77 pounds and 4 ounces.

October 2: Nephritic Test Meal (Mosenthal): Water retention, — + 47 c.c.; nitrogen retention, —0.1 gm.; sodium chlorid retention, —0.69 gm.

October 4: After being out of bed for a few days edema returned.

October 7: Still has edema. Urine about the same since admission. Albumin, three plus; hyaline and granular casts; no erythrocytes or leukocytes.

October 26: Phenolsulphonephthalein test, intramuscular: first hour, 25 c.c. (10 per cent.); second hour, 50 c.c. (15 per cent.); total, 25 per cent.

October 27: Phenolsulphonephthalein test, intramuscular: first hour, 50 c.c. (17 per cent.); second hour, 100 c.c. (15 per cent.); total, 32 per cent.

November 9: On high protein diet.

November 21: Blood pressure, 100/70. Edema and weight about the same.

November 25: Water Test.

November 18: Blood Chemistry: Urea nitrogen, 12; cholesterin, 1.552 per cent.; serum protein, 5.58 per cent.; cells, 30 per cent.; plasma, 70 per cent.

December 7: Basal metabolism, —23 per cent.

December 12: Edema Fluid: Protein, 0.188; specific gravity, 1.010; cholesterin, none; fat, 0.03; sodium chlorid, 0.65.

December 26: Weight, 83 pounds and 13 ounces.

Jan. 10, 1922: For the past four or five days child has been running a temperature with marked abdominal pain. Leukocytes, 23,000; polymorphonuclears, 94 per cent. Signs of pneumonia at the right base with a pneumococcus peritonitis.

January 14: Child died. No necropsy obtained.

Case 8 (Hospital No. 208603).—Male, aged 4, admitted March 12, 1921. During his stay in the hospital had considerable abdominal pain and pain on urinating. Urine, smoky and containing considerable blood. No explanation for the pain. The roentgenograms were negative. The chemistry of the blood showed an increase of nitrogen retention, increase in cholesterin and a marked diminution in carbon dioxid content; this latter due perhaps to the administration of morphin just before admission. While in the hospital he gradually acquired ascites and general edema; then a very severe colitis with mucus and blood in the stools, lasting several weeks. During this time edema and ascites disappeared. When colitis stopped edema reappeared. Finally discharged, June 14, in good general condition; albumin and casts in the urine; increased cholesterin in the blood, but no retention of nitrogen. When reexamined six months later the child was free from edema; urine contained albumin; blood almost 1 per per cent. cholesterin.

TABLE 22.—Urinary Excretion After Water Test in Case 5

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	40	1.030
9:00 a. m.	54	1.006
9:30 a. m.	156	1.002
10:00 a. m.	160	1.001
10:30 a. m.	20	1.008
11:00 a. m.	20	1.010
11:30 a. m.	25	1.012
12:00 m.	16	1.014
3:45 p. m.	92	1.024
6:00 a. m.	320	1.016
8:00 a. m.	190	1.014

Family History.—Negative.

Previous History.—Measles in infancy; tonsillitis and scarlet fever (?) one year ago. No sore throat since.

Present History.—Eight months ago, about four months after the questionable scarlet fever, child's face became swollen, followed by general anasarca. Abdomen tapped. During this time vomited almost every day. After a few weeks the edema disappeared to reappear subsequently two or three times. Two and one-half months ago severe pain in the right side with a temperature of 106 F. Anuria of one day's duration. Following this the urine was bloody for several weeks, and for weeks still had casts in the urine. Six weeks ago blood reappeared and intermittent hematuria has been present ever since. Two days ago child again had sudden pain in the right side with high temperature and anuria. A discharge from the right ear has persisted for the past six weeks.

Physical Examination.—The boy was semistuporous, face puffy and breath uremic. Tonsils: hypertrophied. Tight ear discharging. Heart, negative. No edema of the body or extremities. Catheterized specimen, 420 c.c. Phlebotomy, 100 c.c. Blood pressure, 100/70. Urine, smoky; albumin, two plus. Many erythrocytes and hyaline and granular casts.

Laboratory Examination.—March 12: Leukocytes, 16,000; polymorphonuclears, 75 per cent.; hemoglobin, 57 per cent.; erythrocytes, 3,000,000.

Blood Chemistry: Nonprotein nitrogen, 87.5; uric acid, 4; creatinin, 2.4; carbon dioxid, 17.6; cholesterin, 0.314 per cent.

Temperature, 102 F. Wassermann test, negative.

The semistuporous condition may have been due to the uremic poisoning as there is considerable nitrogen retention. On the other hand there is a very low carbon dioxid content which may point to an acidosis. Yet this might be due to a dose of morphin given just before admission. Child was put on 800 c.c. of 10 per cent. glucose water.

March 14: During the past few days patient's general condition is slightly improved but he complains of abdominal pain and pain on voiding. This latter may be due to the catheterization which was necessary.

TABLE 23.—Urine Excretion in Case 8 After Water Test

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	57	1.010
9:00 a. m.	145	1.002
9:30 a. m.	153	1.002
10:00 a. m.	165	1.002
10:30 a. m.	130	1.002
11:00 a. m.	45	1.002
11:30 a. m.	27	1.010
12:00 m.	27	1.006
Total 4 hours	—— 749	
5:00 p. m.	45	1.016
4:00 a. m.	105	1.018
8:00 a. m.	40	1.014
Total 24 hours	——1,009	

March 17: Sensorium is clear. Blood carbon dioxid, 29.4. Roentgen-ray examination of the kidney region is negative. The phenolsulphonephthalein excretion is 20 per cent.

March 27: Patient's general condition is excellent. On a diet of cereal, toast, spaghetti, fruit, green peas, baked potato and 450 c.c. of fluid consisting of milk only. Thus has a relatively high carbohydrate diet with moderate amount of protein in the form of vegetable and milk protein.

March 30: A water test of 800 c.c. of fluid showed that the first four hour excretion was almost normal, although the concentration was poor.

April 1: Blood Chemistry: Urea nitrogen, 14; nonprotein nitrogen, 46.7; uric acid, 2.6; creatinin, 1.7; cholesterin, 0.616 per cent.; carbon dioxid, 40.4. Total serum protein, 5.6 per cent.

April 8: Under the carbohydrate diet which he has been receiving the blood in his urine had entirely disappeared and edema had also disappeared.

April 11: The edema and ascites again increasing; put on a high protein diet consisting of egg, chicken, green peas, 600 c.c. of milk, small amount of cereal and toast.

April 13: Edema steadily increasing. Weight, April 4, 37 pounds; April 12, 47 pounds.

April 19: First signs of a diarrhea with mucus, blood and pus in the stools. From April 19 to 24 has had attacks of severe abdominal cramps, frequent movements and his ascites and general edema are entirely disappearing. Put on 600 c.c. of protein milk alone. Weight dropped to 40 pounds.

April 26: Still many bowel movements.

Blood Chemistry: Urea nitrogen, 32.2; nonprotein nitrogen, 63; uric acid, 4.4; creatinin, 2.1; cholesterin, 0.496 per cent. Total serum protein, 5.3 per cent. The stool picture shows gram positive bacteria.

April 30: Weight, 33 pounds, 6 ounces. Intake, 1,000 c.c.; excretion, 1,000 c.c. Diet: skimmed milk, hard boiled eggs, toast and split pea soup.

May 6: Still some diarrhea but very much better. Weight, 33 pounds. Excretion very good.

May 11: Phenolsulphonephthalein test, 35 per cent.

Blood Chemistry: Urea nitrogen, 12.6; nonprotein nitrogen, 40 per cent.; uric acid, 4.5; creatinin, 1.5; cholesterin, 0.418.

Child is out of bed and edema has disappeared.

May 12: Child has had temperature of 103 F., and a rapid recurrence of the edema. The urine contains a good deal of albumin and hyalin casts but no blood.

May 21: Blood pressure, 90/40. The ascites and edema are increasing. Stools are good.

May 24: General condition is very poor. Child is drowsy. Uremia (?); ascites and edema increasing.

May 30: Again frequent bowel movements but no blood in the stool.

June 4: Diarrhea is better. Fundi, negative. Hemoglobin, 72 per cent.

June 14: Home. General condition very good. No edema. Albumin and casts in the urine.

November 19: Seen for reexamination. Has had occasional edema of the face. On a high protein and low fat diet all this time.

Physical Examination.—Child has slight edema of the face and pretibial edema; otherwise negative.

Blood pressure, 100/70. Hemoglobin, 60 per cent.

Blood Chemistry: Nonprotein nitrogen, 56; cholesterin, 0.928 per cent.; serum protein, 4.3; cells, 29 per cent.; serum plasma, 71 per cent.

Urine: Albumin, three plus; no casts.

From this it will be seen that although the child was practically free from edema the cholesterin content is the highest yet obtained in this case.

Case 11 (Hospital No. 208275).—Male, aged 3½, admitted Feb. 28, 1921. Observed for nine months with a history of edema of six months' duration before admission. The blood nitrogen has never been increased; the blood cholesterin has always been higher than normal, but lowest on last examination. The total serum protein while in the hospital was 6.2 per cent., but has now dropped to 4.2 per cent. The serum has always been milky. The recurrent edema, the absence of increased blood pressure, the urine and blood findings lead us to classify this as a true nephrosis. This case is especially important since the child had diphtheria just before the onset of symptoms.

Family History.—Negative.

Previous History.—Frequent sore throat and enlarged glands. Diphtheria, ten months before admission; tonsils removed two months after diphtheria. Pneumonia, when 2 years old; measles when 1 year old.

Present History.—Six months ago, that is, four months after diphtheria, child's face became swollen, followed by swelling of abdomen and legs. Since then there has been an increasing pallor and weakness, with hematuria on two or three occasions. No headache, vomiting or convulsions. Meat free and salt poor diet for past six months. About ten weeks ago at another hospital in this city where he remained for four weeks. Taken home with generalized edema and passing about 4 ounces of urine a day.

Physical Examination.—Child chronically ill. General edema. Tonsils have been removed. Heart and lungs: negative. Abdomen: distinct fluid wave. Liver: 3 cm. below costal margin. Extremities: moderate edema.

Laboratory Examination.—Pirquet and Wassermann tests, negative. Hemoglobin, 80 per cent.; erythrocytes, 4,100,000; leukocytes, 12,000; polymorphonuclears, 55 per cent. Blood pressure, 100/80.

Urine: Albumin, three plus; many hyalin and granular casts.

Blood Chemistry: Urea nitrogen, 19.6; nonprotein nitrogen, 53.4; uric acid, 2.6; creatinin, 1.7; cholesterin, 0.592 per cent. Serum, milky.

Diet: Fluids limited to 500 c.c.; milk, cracker and zwieback were given.

March 4 to 10: Salt metabolism estimated. Conclusions of this test are marked water retention, moderate sodium chlorid retention, no nitrogen retention. Intake, 500 c.c. per day; average excretion, 250 c.c.

March 28: Child gradually improving. Put on a diet consisting of cereals, milk, toast and ice cream. Water intake and excretion about the same. Weight, 32 pounds.

TABLE 24.—Urine Excretion in Case 11 with and without Water Test

March 27: Water Test: Intake, 800 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	110	1.012
9:00 a. m.	125	1.003
9:30 a. m.	214	1.003
10:00 a. m.	230	1.002
10:30 a. m.	141	1.001
11:00 a. m.	48	1.008
11:30 a. m.	14	1.012
12:00 m.	18	1.014

Total excretion: 900 C.c.

TABLE 25.—Urine Excretion and Weight in Case 11

Date	Intake	Excretion	Weight
March 4	600	400	31^{8}
March 6	500	150+	30^{8}
March 7	500	470	30
March 13	500	350	32^{3}
March 17	500	400	32^{4}
March 21	560	550	32^{3}
March 27	800	750	32^{12}
March 31	660	700	31^{13}
April 2	855	540	32
April 8	720	750	33
April 9	510	800	33^{4}
April 10	540	800	32^{13}
April 16	500	250	31
April 23	500	225	31^{12}
May 1	500	500	31^{11}
May 8	500	325	32
May 9	500	350	32

Blood Chemistry: Serum, milky; urea nitrogen, 16.8; nonprotein nitrogen, 32.2; uric acid, 2; creatinin, 1.3; cholesterin, 0.696; carbon dioxid, 43.3.

April 26: Child still improving; up in chair. Weight, 31 pounds and 12 ounces.

Blood Chemistry: Urea nitrogen, 16.8; nonprotein nitrogen, 46.9; uric acid, 2.4; creatinin, 1.2; cholesterin, 0.424 per cent.; total serum protein, 6.2 per cent.; serum sodium chlorid, 5.9 mg.

Urine: Albumin, two plus; occasional granular casts.

Blood pressure, 105/85.

May 10: Discharged with the following note: Free from edema. Water excretion about the same as intake. Urine: albumin, two plus, with only a rare cast.

Diet: 500 c.c. of fluid—water and milk—rice or other cereal, potato, vegetables, ice cream. Weight, 32 pounds.

Return Examination.—November 15: Since discharge from hospital six months ago has had frequent puffiness of the face, but no edema of legs or ascites. Has been on above diet since discharge. Has passed about 12 ounces of urine a day.

Physical Examination.—The child is in fairly good condition; pale; some edema about the eyes. Lungs: little dulness at left base. Heart: not enlarged. Abdomen: no ascites. Lower extremities, no edema. Blood pressure, 89.60.

Laboratory Examination.—Urine: Specific gravity, 1.030; albumin, heavy trace; rare casts. Blood Chemistry: Serum, milky; urea nitrogen, 14; uric acid, 2; creatinin, 1; cholesterin, 0.376 per cent.; total serum protein, 4.2 per cent.

Case 13 (Hospital No. 214516).—Male, aged 4½ years, admitted Oct. 27, 1921. Observed one month in hospital with a previous history of five weeks. Only possible etiology was tooth extraction. The intractable edema despite marked limitation of fluid, the normal blood nitrogen, the high cholesterin, the lowered basal metabolism and the urine findings lead us to classify this case as a true nephrosis. A high protein diet tried for two weeks had no effect.

Family History.—Negative

Previous History.—Child frequently had fairly sore throat. Tonsils and adenoids removed two years ago. Measles, two years ago; pneumonia and otitis media, five months ago.

TABLE 26.—Urine Excretion in Case 13 Before and After Water Test

Nov. 4, 1921. Water Test: Intake, 350 C.c.

Time	Volume, C.c.	Specific Gravity
8:30 a. m.	70	1.028
9:00 a. m.	55	1.006
9:30 a. m.	75	1.002
10.30 a. m.	16	1.006
11:15 a. m.	20	1.012
12:00 m.	6	
2:00 p. m.	10	
3:30 p. m.	15	1.020
2:15 a. m.	75	1.032

Total four hours, 242 c.c. Total twenty-four hours, 342 c.c.

Present History.—About five weeks ago had a tooth extracted. Almost immediately after that it was noticed that child had puffiness of eyelids, but in the course of two weeks it had disappeared. About ten days ago the edema reappeared and rapidly involved the body and the extremities.

Physical Examination. — Child chronically ill. General anasarca. Face: edematous. Eyes: almost closed; swelling of the lids. Throat: slightly congested. Lungs: little flatness and diminished breathing at right base. Heart: negative. Abdomen: distended with fluid wave. Marked edema of scrotum and penis. Extremities: marked edema.

Laboratory Examination.—Pirquet and Wassermann test, negative. Hemoglobin, 90 per cent.; erythrocytes, 5,470,000; leukocytes, 17,000; polymorphonuclears, 73 per cent. Blood pressure, 98/68.

Urine: albumin, four plus; many casts and a few white blood corpuscles.

Blood Chemistry: Serum, clear; urea nitrogen, 12.6; nonprotein nitrogen, 32.9; creatinin, 1.2; cholesterin, 0.552 per cent.

Phenolsulphonephthalein Test (intramuscular): Excretion first hour, 12 per cent.; second hour, 8 per cent.; total, 20 per cent.

Diet: Milk, 500 c.c. for four or five days; later reduced to 350 c.c. Weight, 37 pounds and 6 ounces.

November 8: Given thyroid, ½ grain, twice a day. Discontinued after two days.

November 11: Phenolsulphonephthalein Test (intravenous): Total excretion, 50 per cent. after two hours.

November 13: Child had not improved. Weight, 5 pounds more than on admission. Put on high protein diet, consisting of 350 c.c. skimmed milk; two eggs; chicken, 50 gm.; peas, 20 gm.; farina once a day.

November 14: Southey tubes applied to lower extremities; about 60 c.c. of edema fluid obtained. Analysis of edema fluid: specific gravity, 1.005; cholesterin, 0.012 per cent.; sodium chlorid, 0.643 per cent. Basal metabolism, 20 per cent. Blood pressure, 80/60.

CASE 16 (Hospital No. 210059).—Male, aged 2, admitted May 9, 1921. Child has had edema for eight months. Etiology, probably scarlet fever. Has had all modes of treatment, protein free diet, high protein diet, diuresis, thyroid, decapsulation of kidney, without any effect. The urine always contained large amounts of albumin and casts; the blood urea became high during the latter part of the illness. The cholesterin always remained high, but what was most surprising, the serum protein was not decreased. Child finally died. A typical case of nephrosis.

TABLE 27.—URINE EXCRETION AND WEIGHT IN CASE 13

Date	Intake	Excretion	Weight
October 28	...	315	37^{6}
October 29	...	300	
October 30	...	60	
October 31	...	270	
November 1	690	120	
November 2	830	200	
November 3	600	300	42
November 4	360	300	
November 5	550	240	
November 6	600	180	
November 7	300	360	
November 8	30	18	
November 9	30	36	
November 10	390	150	42^{2}
November 11	360	210	42^{5}
November 12	360	90	
November 13	300	420	42^{6}
November 14	360	240	42^{12}
November 15	390	240	42^{14}
November 16	423	150	43^{6}
November 17	330	?	43^{5}
November 18	360	?	44
November 19	420	420	45^{2}
November 20	450	120	45^{3}
November 21	270	270	45^{4}
November 22	480	210	45^{10}
November 23	350	200	45^{11}
November 24	350	85+	46
November 25	350	239+	46^{2}
November 26	350	150+	47
November 27	...	...	47^{2}

Family History.—Three children. Mother had three miscarriages after birth of second child; otherwise negative.

Previous History.—Whooping cough when 7 months old; when 1 year old, fairly severe burn on body which healed in three weeks.

Present History.—About six weeks before admission an older sister of patient had scarlet fever. About this time this child had a mild rash for one day with temperature. One month before admission child fell a great deal, and it was then noticed that his legs were swollen and that he passed very little urine. Urine examined and albumin found but no blood.

Physical Examination.—Patient acutely ill. Generalized edema. Eyes almost closed because of swelling of lids. Ears: purulent discharge from right ear. Throat: tonsils ragged; not congested. Lungs: dulness at both bases. Heart: not enlarged. Abdomen: very much distended with shifting dulness. Extremities: swollen. Weight, 29 pounds.

Laboratory Examination.—Hemoglobin, 74 per cent.; erythrocytes, 5,500,000; leukocytes, 15,400; polymorphonuclears, 60 per cent.

May 9: Urine: specific gravity, 1.030; albumin, four plus; many hyalin and granular casts and rare leukocytes.

Blood Chemistry: Urea nitrogen, 18.2; uric acid, 1.5; cholesterin, 0.376 per cent.; carbon dioxid, 34.7; sodium chlorid, 5.5; serum protein, 5.77 per cent.

Pirquet and Wassermann tests, negative. Blood pressure, 90/60.

Diet: Water, 500 c.c.; sugar, 90 gm.

May 13: Put on high protein diet. Southey tubes were inserted in lower extremities. For next few weeks no improvement in the edema. Blood Examination: Urea nitrogen, 32.2; nonprotein nitrogen, 66.5; uric acid, 2; creatinin, 1.6; cholesterin, 0.532 per cent. Plasma Volume: cells, 24 per cent.; plasma, 76 per cent. Weight, 32 pounds.

June 9: Transferred to surgical service where double decapsulation of kidneys was done. Kidneys, large and pale.

June 25: Transferred to medical service. During stay in surgical ward there was not much change in the edema. Fundi were normal. Blood Chemistry: Urea nitrogen, 23.8; cholesterin, 0.308 per cent. Diet: fruit juices, vegetable, milk, 800 c.c. Within next few days child became very edematous. Diet consisted of 350 c.c. of milk.

July 11: Thyroid, ¼ grain, three times daily, given. One week later gelatin and cream cheese added to diet. This was followed by diarrhea, but edema became less marked. Urine could not be measured, but child was voiding a fair quantity. Two weeks later edema again increased. Put back on high protein diet and 10 grains urea chlorid, given three times a day. Weight, 25 pounds.

August 24: Blood Chemistry: Urea nitrogen, 47.6; cholesterin, 0.360; protein, 7.15 per cent.

September 3: No improvement. Given diuretic.

September 14: Paracentesis, 300 c.c. fluid obtained. Previous diet discontinued; put on 400 c.c. milk.

September 19: Put back on high protein diet.

September 30: Taken home against advice with no improvement. Urine remained the same throughout the entire stay in hospital, containing albumin, four plus, and casts but no blood cells. Discharge weight, 23 pounds, 5 pounds less than upon admission.

A few days later child was taken to Babies' Hospital, New York. No improvement. Child was transfused but died within two weeks.

ORAL DISORDERS IN PEDIATRICS *

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The responsibility of oral diseases must rest on the physician rather than on the dentist, for the dentist and oral surgeon heal and correct already existing oral disorders, while the opportunity of detecting and preventing potential disturbances comes to him whose contact with the patient commences early and continues with more or less frequency.

This is particularly true of the pediatrician; who visiting the patient in most cases shortly after birth assumes the care of the general condition, which naturally thrusts on him the responsibility for the condition of the oral cavity. The widespread interest lately aroused by statistics indicating the large numbers of children affected with teeth disorders, makes it desirable for the pediatrician to become better acquainted with the normal oral cavity, so that he may detect earlier any abnormal conditions or tendencies in the child's mouth. With these facts in mind, it may be profitable to examine anew some of the more common oral disorders.

Formation of Teeth.—Preparation for tooth formation takes place as early as the sixth week in utero, and between the seventh and eighth week, the first step in development is evident by the formation of what is known as a dental band or ridge. The enamel begins to form on the deciduous teeth about the seventeenth week in utero and ends about six months after birth.[1] It is evident, then, that the pediatrician has almost no control of the formation and general condition of the deciduous teeth. The condition of the primary teeth is practically settled before birth.

The formation of the teeth of the unborn child may be impaired in one or two ways: (1) by lack of suitable material with which to form teeth, and (2) by impairment of formation by toxemias. It is obvious that the fetus needs the salts of calcium and phosphorus in the formation of teeth, and it must depend on its mother for that supply. Vitamins are most essential so that their salts may be utilized. Therefore, besides other essentials necessary to attain proper metabolism, the mother should have a well balanced diet, giving special attention to those foods which contain mineral salts and vitamins if good deciduous teeth are to be formed.

Although the tissues of the mother, rather than the tissues of the unborn child, suffer from any acute or chronic toxemias, nevertheless these toxemias probably cause serious impairment of the formation of

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tissue because of its disturbances of metabolism, and consequently lessened assimilation of food. This naturally includes a diminution in the amount of available salts to be utilized in the formation of teeth. Another result of toxemia which also leads to a defective formation of teeth is anorexia. Hence it is important that all sources of toxemia in the mother should be eliminated as far as practicable. Dental decay often leads to toxemia in pregnant mothers. Only a small percentage of these mothers state that they received any treatment for dental decay. Of course, it would be far better if these pathologic dental conditions were discovered and treated before pregnancy occurred. Nevertheless, pregnancy is no barrier to dental treatment. About 75 per cent. of the mothers of the children attending the preventive clinic give a history of some dental ailment. With the exception of decayed teeth, most of these ailments disappear at the birth of the child, and reappear with subsequent pregnancies.

Dr. Percy Howe's animal experiments in the research laboratory of the Forsyth Dental Infirmary, have shown that lack of proper diet has some bearing on dental ailments, particularly when the teeth begin to loosen. Perhaps, the loosening of teeth may be the result of a drain by the fetus on the maternal supply of phosphorus and calcium. If this supply is not furnished through the diet of the mother, it is natural to assume that the maternal tissues, particularly the teeth and bones, will suffer, since they will be required to contribute the necessary elements for the bone and teeth formation of the unborn child.

Of the permanent teeth, the enamel begins to form at birth or shortly before birth with the first molar, and the complete formation of the enamel of all the permanent teeth is complete about the twelfth year on the crown of the third molar. After the fifth year, however, only the second and third molars have the formation of their enamel completed.[1]

The formation of teeth, both temporary and permanent, is subject to many disturbances, particularly those of infection and nutrition. The temporary teeth, as compared with the permanent teeth, show very little defects in their formation.

The formation of enamel proceeds at fairly regular intervals. Any temporary cessation of this process can usually be recognized, even to the time of occurrence, by noting the various defects in the enamel of the teeth undergoing calcification during that period. The effect of malnutrition on the teeth shows itself through many defects. Since the enamel is derived from the epithelium, and is also ultimately derived from the epiblastic germ layers,[1] the eruptive diseases, notably scarlet fever and measles, leave their imprint on the enamel of the teeth. In fact, any febrile condition of more than three or four days' duration seems to leave its mark on the formation of the enamel. Defective enamel formation usually occurs in rickets.

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[1] Endleman, O., and Wagner, R. F.: General and Dental Pathology, St Louis, C. V. Mosby Company, 1920.

Such defects as the chalky appearance of the enamel, pitting, transverse bands on the surface, brown staining of the enamel, irregular and serrated edges of the teeth, are seen with very great frequency at the clinics. These are the result of constitutional diseases and malnutrition.

Dentition.—There is altogether too great a tendency on the part of the pediatrician to disregard the diagnosis of dentition. Dentition or teething should be regarded as a physiologic process and should proceed without any disturbances. Clinical evidence, however, does not always support this view. Unfortunately, a diagnosis of "teething" is often made either from neglect to perform a complete physical examination, or from inability to interpret properly the findings of such an examination.

H. Able states that a connection between febrile affections and dentition does not exist, but many febrile diseases lead to an increased eruption of teeth, in the same way as the increased growth of children occurs during or after febrile disorders, through the stimulating action of toxins on the epiphysis. He made observations on nineteen cases of measles in children under 2 years of age who showed an extraordinary increase of erupted teeth during the time of febrile attack and immediately afterward.[2]

There is an abundance of clinical evidence to show that the diagnosis of dentition can be made correctly in many instances. Kirk[3] states that the harmonious synchronism between root growth and tissue absorption is a delicately balanced mechanism, and a sort of moving equilibrium depending for its stability on the nutritional and physiologic balance of the entire organism. There is harmonious correspondence between the addition by growth to the developing root of the teeth and the absorption of the tissues overlying the tooth crown as the eruption of the tooth proceeds. Pain, which is a frequent accompaniment of teething, although this is difficult to prove, is caused not by pressure of the tooth on the gums, but rather by the pressure of the gums on the tooth, which, in turn, presses on the underlying nerves.

The evidences of teething may vary. Symptoms such as rise in temperature, disturbed sleep, gastro-intestinal disturbances (particularly diarrhea), increased salivation and increased desire for water, are common. The weight curve may be disturbed. In babies who show evidence of spasmophilia, convulsions are very common with teething. Often babies who previously offered no resistance to examination of the mouth will, when teething, oppose any attempt to open the mouth for examination, keeping the lips very firmly compressed. The gums in the areas where teeth are to be erupted are tender and may appear slightly swollen, either red or, more often, white in color. The baby frequently has a desire to bite on anything, and finds relief in this way. This tendency disappears when the teeth are erupted. Otitis media and bronchitis are said to be frequent accompaniments of teething; this may be due to a lowered resistance caused by physical irritation. It is commonly accepted that physical irritation from adenoids, phimosis and pin worms may cause constitutional disturbances. These disappear with the removal of the cause, and may be favorably compared to the disappearance of the symptoms after the teeth erupt. Dentition may sometimes have a marked effect in increasing the irritability of the nervous system, more especially in infants having rickets, spasmophilia or some nervous disorders.

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[2] H. Able: Wien. klin. Wchnschr., No. 14, 1919, p. 392.

[3] Kirk, E. C.: Dental Cosmos **62**:1373 (Dec.) 1920.

The evidence that these symptoms are due to dentition alone is, first, that the symptoms disappear, often with remarkable suddenness, immediately after the teeth erupt, and second, that with the eruption of other teeth, similar symptoms appear.

Hygiene of the Mouth.—Oral disorders, especially in the first months of life, frequently result from practices which are thought to be required by good hygiene. The epithelium of the mouth of the infant in the early months is very sensitive to trauma. Even the slightest trauma may be followed by infection. It has been demonstrated repeatedly that infants who do not receive any mouth cleaning before the eruption of the first tooth show a healthy epithelium and do not suffer the various forms of stomatitis peculiar to early infancy. No matter how carefully the finger is introduced into the mouth for cleansing purposes, nothing but harm can possibly result from such practice. A toothless mouth requires no cleansing.

Trauma plays an important part in the etiology of stomatitis occurring during infancy. The giving of food which is too hot or unclean also causes stomatitis. If more attention were paid to proper cleansing of nipples, and to avoidance of the introduction of soothers and other unnecessary objects into the mouth, there would be fewer cases of stomatitis in infancy.

The principles of the hygiene of the mouth containing teeth are still uncertain. The doctrine that a clean tooth never decays is not borne out by clinical evidence. It may be nearer the truth to state that a clean tooth may not decay as rapidly as one that is not clean. Tooth powders and pastes, mouth washes and alkaline dentifrices, and other cleaners, chemical or mechanical, are recommended by many authorities for the prevention of oral disorders. It has been shown that antiseptic washes act only while they are in the mouth, if they act at all; five minutes after their use cultures show growth.[4] Weak acid washes act to better advantage than alkaline washes by increasing salivary secretion. Antiseptic washes, on the other hand, are salivary depressants.[4] As far as tooth powder and tooth pastes are concerned, there is no direct evidence to support the claims that they prevent decay. Cameron[5] has shown that a well shaped tooth has no food residue ten minutes after soft pultaceous food has been consumed. It is the belief of some dental authorities that teeth are self-cleansing. Many uncivilized peoples have clean teeth despite the fact that they have never even seen a tooth brush. Some of these people rub their gums with the fingers or cause friction on their gums mechanically by choosing foods that require a great deal of mastication. Some barbarians who are said to eat very soft mushy food, and eat only twice daily, have clean oral cavities. This may be explained by the fact that their foods contain an abundance of vitamins and are well supplied with salivary activators.

Carious Teeth.—There is hardly any one factor more striking today than the marked prevalence of carious teeth among civilized people. The fact is all the more remarkable in that as soon as civilization creeps into any community hitherto without its blessings, the number of those affected with carious teeth greatly increases. Statistics have demonstrated how vitally carious teeth affect the nation. Dental defects were second in importance as a cause for physical rejection in the United States Army. This is a sorry showing that cannot be laid entirely to the dental profession. The fact that school records show that toothache is one of the most frequent causes of absence,[6] suggests the seriousness of the situation. In the children's clinics of every city, the presence of a child having a well formed set of teeth with little or no caries, or only one or two teeth missing, usually excites comment from the examiner. I have reviewed the literature on carious teeth, and have been surprised to learn how little is known about the prevention of caries. Hipprocates, in 500 B. C., wrote that caries is a manifestation of stagnation of depraved juices. Other causes such as inflammation, worms, putrefaction, chemical disolution, parasites, drugs, decomposition, various kinds of foods,[7] micro-organisms,[8] and osmosis[9] have been considered at one time or another since then. In 1881-1901 the chemico-parasitic theory of Miller seemed to have settled beyond doubt to most members of the dental profession that the cause of carious teeth had been solved, and henceforth prevention of caries was a comparatively simple process, i. e., by the removal of the cause of fermentation locally. This theory has been convincingly disproved by Howe and others.[10] It is due to the persistent efforts of Drs. J. Sim Wallace and H. C. Pickerill[4] of England and Drs. Percy Howe and W. J. Gies of this country that the theory of diet being a controlling element in the causation of carious teeth is gaining support. Other influences may be responsible for the increase in the number of carious teeth, such as environment, manner of living, and infection. The evidence, however, seems to point toward defective diet as being largely responsible for the widespread prevalence of carious teeth.

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[4] Pickerill, H. P.: The Prevention of Dental Caries and Oral Sepsis, London, Bulliere, Tindall and Cox, 1919, p. 265.

[5] Cameron, H. C.: Lancet **1**:86 (April 23) 1921.

[6] U. S. Public Health Rep., Nov. 19, 1920, p. 2763.

[7] Baker, A. W. W.: Tr. Roy. Acad. Med., Ireland **10**:355, 1891.

[8] Walkhoff: Brit. J. Dent. Sc. **64**:212 (July) 1921.

[9] Echerman, R.: Dental Items of Interest **40**:466 (June) 1918.

The following, gathered from the literature on carious teeth, are the usual illustrations which point to diet as a causative factor of caries:

1. Teeth of primitive people in Australia, who for many years have lived under civilized or partially civilized conditions, are bad in comparison with those of their tribe who have continued under primitive conditions.[11]

2. Kaffirs supplied with the food of civilization have in one generation become totally different, in regard to caries, from those Kaffirs who are still living on their native diet.[1]

3. The disease is rare among the Red Kaffirs in southeastern Africa who have not taken kindly to European conditions and diet.[12]

4. The Esquimaux were practically free from caries until change of diet with the influx of refined food.[10]

5. Colyer notes that men of certain tribes of Africa did not have dental caries until they were recruited into the British Army.[13]

6. The Maori children in New Zealand have the very low rate of 1 per cent. caries. In Europe the rate for carious teeth is 85 per cent.[14]

7. In Scotland, among those living on the highlands and using coarse foods, caries is rarely seen. Those who inhabit the lowlands and partake of the finer foods suffer far more from carious teeth.[15]

At a clinic held in June, 1921, during the annual meeting of the American Medical Association, at the Forsyth Dental Infirmary, Dr. H. DeW. Cross presented 176 immigrant children of all ages, all of whom had been in this country less than four weeks. Almost all nationalities were included in this group, except those of English, Irish or French descent. Virtually none of these children had ever seen

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10. Howe, P.: Dental Cosmos **42**:921 (Aug.) 1920.
11. Suk, V.: Am. J. Physical Anthropol. **2**:351, 1919.
12. Colyer, S.: Brit. Dent. Rec. **39**:401, 1919.
13. Colyer, S.: Brit. Dent. Rec. **37**:405, 1917.
14. Gibbs, J. H.: Edinburgh M. J. **18**:433 (June) 1917.
15. Wells, F. M.: Brit. J. Dent. Sc. **14**:135 (May) 1921.

a toothbrush. Dr. Cross found that 30 per cent. had perfect mouths, 30 per cent. had no more than two small cavities, and a bad mouth was the exception among the remainder. In contrast to this, I presented almost an equal number of children, of about the same ages, all being born in this country. They showed little or no evidence of malnutrition and had been chosen at random, just as were those of the other group. In this group a perfect mouth was the exception; about 80 per cent. of these children showed mouths in need of dental treatment. A few of the mouths were almost beyond repair. A large proportion of these children had been under a physician's care since birth. Needless to mention, these school children were well versed in the art of using the tooth brush, and a great majority of them presented the so-called physiologically clean mouth, but had carious teeth, while many of the "new Americans" of Dr. Cross's group had tartar on their teeth, but were free from caries.

Since our knowledge of etiology of caries is insufficient for its prevention, early treatment is of paramount importance. It has been conservatively estimated that more than 90 per cent. of the children entering the public schools are in need of treatment for carious teeth. No doubt, a large proportion of these children had already been seen, for one reason or another, by a physician, and caries noted yet comparatively few show any evidence of dental treatment. Instead of early decay being arrested, the condition is allowed to go from bad to worse.

Early decay is first seen at the junction of the teeth and gums. If the pathologic condition of the teeth is so far advanced that the tooth does not function, then extraction is strongly advisable. A badly decayed tooth does not function because the child will not chew on it, to avoid the pain caused by the exposed pulp. This leads to bolting the food. Extracting badly decayed temporary teeth conserves the permanent teeth which are in the process of formation, and inflammation around the apex of deciduous teeth will lead to permanent changes in the secondary teeth directly underneath.

Discussion of the necessity for treatment of deciduous caries would be unnecessary were it not for the fact that its treatment is sadly neglected and postponed. Mothers are asking for treatment of their children's first teeth, only to be told that it is impractical and inadvisable because these teeth are only temporary, and are soon to be replaced by permanent ones. Sometimes, the excuse given for not extracting decayed deciduous teeth is that the jaw will not develop properly. These and many other unwarranted excuses are being given to mothers daily both by the dentist and the physician. It is the opinion of those who are in the best position to judge, that any harm that may possibly result from the extraction of carious deciduous teeth is negligible, in comparison to the harm resulting from the failure to extract. Since no child is too young to have caries, it follows that no child is too young for treatment.

No cavity is too small to be disregarded, and the pediatrician should insist on the immediate treatment of caries at any age. It is only by taking care of the teeth of children of preschool age that the teeth of the school children and adults will be safeguarded. The time may be approaching when public schools will demand as necessary for admission a certificate of a clean mouth requiring no dental treatment.

The pediatrician should be aware of the fact that conditions existing during the period from birth until the sixth year determine the future condition of the teeth, all the teeth being already in formation, except the second and third molars, which are formed after this period. In other words, the question as to whether the child's teeth may become carious is practically settled before the eruption of the first permanent tooth, which occurs at 6 years. It is not generally recognized by the pediatrician that the first years of a child's life are critical ones as far as structure of the permanent teeth are concerned.

Diet and exercise of the jaws and teeth are essential, more especially under 5. Dr. W. J. Gies [16] states that since the teeth are formed principally from the salts of calcium and phosphorus, these salts should be given in sufficient quantities in the diet so that teeth will develop as they should. Dr. Percy Howe [17] emphasizes that in order that the body may be able to assimilate the calcium and phosphorus, vitamins are a very necessary addition to the diet. Mrs. May Mellanby suggests [18] that fat soluble A or some other vitamin of similar origin is essential to the diet, before calcium can be used to the extent necessary for the construction of normal teeth and jaws. Dr. J. Sim Wallace insists that the teeth and jaws be made to function through mastication.[19] He believes that soft, mushy foods do not exercise the jaws sufficiently nor stimulate the gums, and that food which requires mastication causes friction in the gums and produces a hard healthy condition. Besides urging that food be hard enough to cause vigorous mastication, Pickerill advocates the use of food that will increase salivary secretion.[4]

Although no one factor can account for the prevalence of caries, it seems reasonable to suppose that the dietary solution of the problem of carious teeth centers about:

First.—The daily intake of foods that contain those substances from which teeth and jaws can be formed, namely, sufficient calcium and phosphorus.

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[16] Gies, W. H.: Dominion Dent. J. **33**:163 (May) 1921.

[17] Howe, P.: Dental Cosmos **63**:1086, (Nov.) 1921.

[18] Mellanby, M.: Brit. J. Dent. Sc. **64**:70 (March) 1921.

[19] Wallace, J. S.: Brit. Dent. J. **32**:415, 1911.

Second.—Adding vitamins to the diet so that the body may be able to utilize these elements. Fortunately, foods that contain an abundant supply of calcium and phosphorus usually contain vitamins also.

Third.—The development and proper functioning of the jaws and teeth, which can best be accomplished by vigorous mastication, therefore, hard and fibrous foods are desirable in the diet.

Fourth.—The stimulation of salivary secretion is necessary if the teeth are to be assured of any benefit that may come from a copious flow of saliva; this can be best accomplished by including in the diet foods that are classed as salivary activators.

A great deal of mineral matter is lost by the methods of preparation in cooking. After vegetables are boiled, the water containing a good deal of the mineral salts is usually discarded. Cereals are ground fine, by high milling, which causes the removal of mineral matter by the finer machinery. White bread, which is made of fine flour, is used extensively instead of common whole wheat bread. These, and many other illustrations show that our modern dietary fails to meet the vital needs of the body.

The preventive clinic at the Forsyth Infirmary recommends cereals such as Irish oatmeal, rolled oats, cracked wheat, cracked corn, hominy grits, brown rice, and others for common usage. There is less destruction in them of the very valuable minerals, and they require more thorough mastication.

As substitutes for the commonly used bread made of fine white flour, the use of whole wheat, rye, bran and oatmeal breads is strongly advocated for their coarser qualities. Rye and whole wheat flour are recommended for home baking. In place of the finer sugars, molasses, honey and pure maple sugar can be substituted to advantage.

Animal experiments have proved that calcium is indispensably necessary to teeth formation. Children who inhabit regions that have excessively soft water show an excessive number of cases of caries.[20] Children living in regions with water containing calcium salts, carbonates or sulphates, have much better salivary glands than those who have grown up in soft water regions; also, the former have less caries than the latter.[21]

Howe has demonstrated that caries can be prevented and arrested by diet alone.[10] By feeding animals with a diet deficient in vitamins, caries and decay readily follow. He has shown, also, that the teeth are one of the first and sometimes the only tissue to be affected by a diet deficient in antiscorbutic vitamins. Vitamins themselves do no apparent good so far as the teeth are concerned if there is an insufficient amount of calcium in the food.

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20. Cook, J. B.: Lancet **1**:888 (March 28) 1914.
21. Rose, C.: Deutsch. Monatschr. f. Zahnh. (Jan.-Aug.) 1908.

Wallace has reported very favorable results in prevention of caries in children by giving a diet containing hard foods. The children developed strong jaws as a consequence of repeated functioning of the masticating apparatus.

It is highly probable that saliva contains a substance or substances to prevent either the onset or the progress of caries. It is interesting to note that saliva of mouths having good teeth has a higher percentage of calcium than saliva of mouths having caries.[4] This may be another means of determining whether or not the body is able to fulfill its calcium requirements. It may not be out of place here to compare calcium deficiency in saliva to endocrine insufficiency. By that is meant that if the body is not supplied with a sufficient amount of calcium, either because of insufficient intake or through a failure of the body to utilize the ingested calcium because of some disturbance in metabolism, the saliva may be taken as an indicator, to some extent, of the calcium content of the body. Likewise, if there is a dietary deficiency, there is every reason to expect a deficiency in the functioning of all the glands of the body. This deficiency includes an endocrine insufficiency, since in proportion the more highly specialized tissues are usually the worst sufferers in any constitutional disturbances. Assuming, therefore, that the body has a sufficient supply of available mineral salts, the mouth can best be supplied with these through stimulation of its gland products, that is, through stimulating the secretion of the salivary glands.

The more saliva that can be stimulated in a natural manner, the more probable it is that there will be sufficient protective agencies. The most natural salivary stimulants are foods, and the character and quantity of saliva depends on the character of food. The salivary secretion does not respond in the same way to all foods. For example, dry bread increases the amount of saliva two to one, apples and oranges increase the saliva six to one. Acids and highly flavored foods increase the saliva in quantity, alkalinity and ptyalin content. Probably all three have much to do with the cleansing of the mouth and prevention of caries. Almost all vegetables, cooked or raw, and all fruits stimulate the flow of saliva. Moreover, when these foods are eaten, the flow of saliva continues long after they are swallowed. The celluloses arrested in the mouth are disintegrated by the teeth; the acidity, remaining long enough in the mouth after the food has been swallowed, is strong enough to continue to simulate the flow of saliva. Other food stuffs besides fruit and vegetables that may be classed as salivary activators are crusts of bread, toast, zwieback, coarse biscuits, nuts, vinegar, sardines and salads. Foods that are known to be poor salivary stimulants include farinaceous foods, fine white bread, fine white biscuits, tea and coffee, alkaline foods, sweets, chocolate, manufactured sugar and tasteless food. Foods classed as indifferent to salivary stimulation include meat, fish, eggs, rice and brown bread.[22]

It has been stated that caries has increased with the increased consumption of refined sugar and commercial glucose used in jams, sweets and syrups. Curiously, these are known to be salivary depressants. According to Wheatley, between 1919-1920, children from Shropshire, 5 years of age, showed on an average 1.9 decayed teeth per child, as against 6.4 per child between 1910-1914. This seemed to be explained largely by the restriction in the purchase of carbohydrates and by the fact that new bread was prohibited and crusts of coarse bread had to be eaten. In poor districts a half penny worth of raw carrot (a vegetable particularly rich in vitamins) largely replaced the prewar penny worth of sweets.[23]

At the preventive clinic a suitable diet is prescribed according to the digestive capabilities of the child, which includes a sufficient amount of calcium and phosphorus, foods containing vitamins, coarse foods that require vigorous mastication, besides foods which are salivary activators. In order to make these foods more palatable and digestible, an expert dietician is to present practical demonstrations in the art of cooking to the mothers. Children frequently refuse to eat fruit, vegetables, and other foods which are most essential for their food values in addition to their salt and vitamin content. This difficulty is largely due to the inability of the mother to make the food attractive or palatable enough to tempt the child's appetite. In addition, this demonstration will have economic value since it stresses food conservation and recommends only the use of foods in season.

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22. Baldwin, H.: Brit. Dent. J. **17**:218 (March 11) 1921.
23. Hendley-Read, E.: Dent. Rec. **41**:185 (April 19) 1921.

AN EPIDEMIC OF STREPTOCOCCUS HEMOLYTICUS SEPTICEMIA *

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The purpose of this report is to record an epidemic of streptococcus septicemia occurring late in November and early in December, 1921, in a ward of seventeen babies in a nursery home.

The age of these infants ranged from one month to 7½ months. They were housed in a new building in a commodious ward, well ventilated and well lighted, with a sun porch attached, where they spent the day in individual cribs and were returned to their beds in the ward at night.

Before the onset of the epidemic all the babies were in good general condition, gaining in weight and having no gastro-intestinal disturbance. All were bottle fed babies, on whole milk dilutions with water and sugar added. Two were receiving small amounts of breast milk in addition to their cow's milk formulas. The milk and water used was boiled three minutes.

Suddenly, as it were out of a clear sky—two of the youngest infants (aged 1 month and 2 months, respectively) began to have fever, one 103 F. and the other 104 F. For the next two days their temperatures ranged from 103 to 105 F., coming down to 102 F. on the fourth day—the day of their death.

Clinically, both children showed extreme prostration, an acutely inflammed pharynx, enlarged cervical glands; on the third day distention of the abdomen with paralysis of the intestines; stupor and death on the fourth day. One infant showed some retraction of the head on the third day. There was no vomiting and no diarrhea. Enemas were given daily. Both infants took their food eagerly until the day of death. There were no convulsions. Nothing abnormal was found on examination of the heart and lungs.

The necropsy findings were: Case 1: Septicemia; peritonitis; cloudy swelling of viscera; hypostatic congestion of lungs and pericardial effusion. Case 2: Septicemia; cloudy swelling of viscera; punctate hemorrhage of renal capsule with a little bloody fluid in the peritoneal cavity.

During the next two and one-half weeks, seven other infants developed symptoms and clinical findings similar to the above, but with the absence of the extreme prostration, the marked pharyngitis and

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cervical adenitis. Five of these seven infants died, and at necropsy the picture was the same as in the first two cases recorded. The degree of pathologic change seeming to be directly proportional to the duration of the illness (Table 1).

Blood was taken from the longitudinal sinus in six of the cases and cultured in sugar agar and sugar bouillon. The *Streptococcus hemolyticus* was recovered in five cases. No attempt was made at further classification of the streptococcus other than to note that it belonged to the hemolytic group. Of the two infants who eventually recovered, one showed a positive and the other a negative culture. All of the seven infants that died and came to necropsy gave positive cultures of the *Streptococcus hemolyticus* from the heart's blood. In one case (Case 4) cultures taken from the heart's blood, pericardial fluid, pleural fluid and peritoneal exudate showed the *Streptococcus hemolyticus* in pure culture.

TABLE 1.—NECROPSY FINDINGS

	Case						
	1	2	3	4	5	6	9
Septicemia	+	+	+	+	+	+	+
Peritonitis	+	..	+	+	+	+	+
Cloudy swelling of viscera	+	+	+	+	+	+	+
Bronchopneumonia	..	..	+	..	..	..	+
Hyperemia of lungs	+	..	..	+	+	..	..
Edema of brain	..	..	..	..	..	+	+
General lymphoid hyperplasia	..	..	+	+	+	+	..
Pericardial effusion	+	..	..	..	..	..	+
Punctate hemorrhage of renal capsule	..	+	..	..	..	..	..

TABLE 2.—CLINICAL DATA

Case	Name	Age in Mo.	Fever	Prostration	Pharyngitis	Adenitis, Cervical	Distended Abdomen	Retraction of Head	Late Stupor	Leucocytosis	Blood Culture	Duration of Disease Days	Result
1	Gordon	1	+	+	+	+	+	+	+	..	..	4	Death
2	Marion	2	+	+	+	+	+	0	+	..	..	4	Death
3	Lena	1½	+	+	0	0	+	+	+	Slight	..	4	Death
4	Eleanor	3½	+	0	0	0	+	0	+	+	+	9	Death
5	Dean	4½	+	0	0	0	+	0	+	+	+	13	Death
6	William	4½	+	0	0	0	+	0	+	+	+	10	Death
7	Leo	4	+	0	0	0	0	+	0	+	0	6	Recovery
8	Martin	3½	+	0	0	0	0	0	0	+	+	10	Recovery
9	Norma	7½	+	0	0	0	+	+	0	+	+	5	Death

The leukocyte counts varied markedly in different patients and during the course of the disease in the same patient, without bearing any remarkable relation to the duration of the disease, the amount of prostration, or the ultimate outcome. These counts varied from 10,000 to 44,000 per cm. The average leukocyte count during the disease, as shown by thirty counts taken from seven patients was 22,650 per cm.

The average differential count taken soon after the onset of the cases was: Polymorphonuclear neutrophils, 52.6 per cent.; basophils, 0.3 per cent.; eosinophils, 0.3 per cent.; small mononuclears, 40.1 per cent.; large mononuclears, 3.1 per cent.; transitionals, 3.3 per cent.

A composite clinical picture of the disease may be summed up as follows:

An infant of the average age of 3½ months, previously well, has a sudden rise in temperature, moderately inflamed pharynx, leukocytosis of about 22,000, a blood culture positive for the *Streptococcus hemolyticus*, a distended abdomen, stupor occurring late (or not at all) and death intervening on about the sixth day of the disease. Cervical adenitis and retraction of the head may also be present (Table 2).

Other babies in the ward showed slight variation from the normal in their temperature records, but not enough to be classed clinically as having the disease. Only one blood culture in this group was taken and it was negative.

At the onset of the epidemic, throat cultures were taken from four of the sick infants and a pure culture of *Streptococcus hemolyticus* was recovered from three while the fourth showed a short gram-negative bacillus together with the *Streptococcus hemolyticus*. A vaccine was prepared from these throat cultures and administered as a preventive to the well babies and in the treatment of the sick.

The entire nursery was put under quarantine and a strict isolation of the sick was instituted at the onset.

Treatment was, in the main, symptomatic. Sodium-bicarbonate was given both by mouth and by rectum. Stimulation with camphor in oil, caffein and digitalis was used. Salt solution was not administered intraperitoneally owing to the ever present abdominal distention and the complicating peritonitis. In one case stock antistreptococcus serum (20 c c, subcutaneously, in two doses) was given without any apparent change in the clinical course of the disease. Both the well and the sick received small doses of the autogenous vaccine every other day. Its effect on the sick was not striking, but it is possible that the giving of this vaccine to the well babies may have aided them in building up an immunity to the disease.

An effort was made to determine the source of the infection. The milk cultured showed no *Streptococcus hemolyticus*. In addition it was the custom to boil all the milk and water used in feeding for at least three minutes.

Cultures were taken, separately, from the throat and nose of each adult (twenty-two in all) connected with the institution. They showed about the usual incidence of *Streptococcus hemolyticus* in the throats of normal adults. Only two persons showed an abundant growth of the *Streptococcus hemolyticus* from both the nose and throat. These two adults had no part in directly caring for the infants of this particular ward nor did they come in contact with their food supply. However, they mingled, when off duty, with those in direct charge of these infants at the onset of the epidemic. One of these "carriers" was removed from the nursery for a period of two weeks. Since her return (more than three months ago) there has been no new case. In fact, the whole epidemic from the beginning to the end was of only three weeks' duration.

To sum up the more striking features:

1. *The suddenness of the onset of an epidemic of Streptococcus hemolyticus septicemia in a ward of seventeen babies all of whom were previously in good physical condition.*—In 1918, when the *Streptococcus hemolyticus* came in for such strong incrimination as the great etiologic factor in respiratory infections, there were, as a rule, predisposing diseases of various sorts, such as measles, influenza and pneumococcus pneumonia, which broke down the resistance of the body and prepared the way for the invading streptococcus (MacCallum,[1] and Blake[2]). In the cases here reported no predisposing disease was present.

2. *The absence of vomiting and diarrhoea.*—These symptoms are frequent complications of all acute infective processes in infants, yet in this group of cases they were entirely absent.

Epidemics of diarrheal diseases due to the streptococcus have been reported (Wilson[3]).

One might suppose that harboring virulent streptococci in the throat, on swallowing these organisms a definite gastro-enteritis would result. Davis,[4] investigating experimentally the fate of the *Streptococcus hemolyticus* in the gastro-intestinal canal, showed that this organism does not develop appreciably in the intestine, nor does it readily gain a permanent foothold there.

3. *The absence of any apparent localized infection or site of primary infection.*—Exception to this is made in the case of the first two cases reported; both babies showed marked pharyngitis and cervical adenitis.

Fox and Hamburger,[5] reporting a streptococcus epidemic following measles, note that it would seem more likely that the process was a primary septicemia, although the infection atrium is clear in no case.

4. *The absence of pulmonary involvement, at least until very late in the disease.*—This, in spite of the fact that bronchopneumonia, as MacCallum[1] and Longcope[6] have reported, was so prevalent in the streptococcal epidemics in the Army camps in 1918.

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[1] MacCallum: J. A. M. A. **71**:704 (Aug. 18) 1918.

[2] Blake: Ann. Otol., Rhinol. & Laryngol. **28**:361, 1919.

[3] Wilson: War Med. **2**:556, 1918.

[4] Davis: J. Infect. Dis. **26**:171, 1920.

[5] Fox and Hamburger: J. A. M. A. **70**:1758 (June 8) 1918.

[6] Longcope: War Med. **2**:566, 1918.

5. *The generally good appearance of the patient until very near the end, thus belying the seriousness of the disease.*—Clinically, this possibly was the most striking feature, and were it not for the fact that positive blood cultures had been obtained, a good prognosis might have been given on the physical findings, when in reality the patient was near death. It leads us also to believe that many of our so-called ordinary "flu" infections are in reality septicemias.

6. *The uniformity with which positive blood cultures were obtained.*—In six patients, with clinical evidence of the disease in which blood cultures were taken, five, or 83 per cent., gave positive cultures for the *Streptococcus hemolyticus.*

Blanton, Burhans and Hunter [7] state:

> The infrequency of septicemia accompanying other localizations of streptococci in the body has frequently invited remark. On many occasions organisms have been recovered from blood at necropsy which repeated cultures had failed to reveal during life.

Davis and Rosenow,[8] reporting the Chicago epidemic of streptococcus sore throat in 1912, found that blood cultures were almost always negative.

Keegan,[9] reporting a hospital epidemic of streptococcic sore throat with surgical complications, obtained negative results from blood cultures.

Only one case of streptococcus septicemia was encountered by Nobécourt and Gimbert [10] with bacteriologic examination of the blood in 600 cases among 3,000 soldiers in more than a year.

Abderhalden [11] obtained 57 per cent. positive blood cultures in fifty cases of septicemia.

Longcope,[6] pointing out the relation of the *Streptococcus hemolyticus* to pneumonia in the troops in the United States, says that blood cultures gave no growth.

However, Wilson [3] reports obtaining the streptococci from blood cultures in twenty out of twenty-three cases.

7. *The marked uniformity with which peritonitis was encountered.*—Clinically this was manifested by a distended tympanitic abdomen, with late paralysis of the intestine, but without the characteristic vomiting and tenderness. It did not appear as an "acute abdomen."

MacCallum [1] says, in regard to the pathology of the epidemic of streptococcal bronchopneumonia in the Army camps, that "peritonitis occurred only twice."

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[7] Blanton, Burhans and Hunter: J. A. M. A. **72**:1520 (May 24) 1919.

[8] Davis and Rosenow: J. A. M. A. **58**:773 (March 16) 1912.

[9] Keegan: J. A. M. A. **72**:1434 (May 17) 1919.

[10] Nobécourt and Gimbert: Bull. Soc. méd. d. hôp. de Paris **41**:1037, 1917.

[11] Abderhalden: J. A. M. A. **67**:236 (July 15) 1916.

Irons and Marine,[12] reporting on streptococcal infections following measles and other diseases, cite two cases occurring in the course of measles with primary peritonitis.

The only clear cut account of a case in a child found in the literature is that of a girl, 6½ years old, reported by MacLennan and McNee [13] in 1913, who had a primary *Streptococcus hemolyticus* peritonitis with septicemia. This occurred after an attack of measles and presented the clinical picture of an "acute abdomen." Operation was performed and a general peritonitis was found with a normal appendix. No localizing cause for the peritonitis was revealed. Pus from the abdomen and blood culture showed the *Streptococcus hemolyticus.* The patient recovered.

8. *The epidemiologic study.*—That pathologic streptococci of the hemolytic group can be conveyed by milk is common knowledge (Davis,[14] Jones,[15] Salter [16] and others). Milk was apparently not a factor in the spread of the present epidemic as a great many more children taking the same milk were not affected. Also, the cases did not have their onset simultaneously, and, finally, the milk used was always boiled and when examined bacteriologically gave negative cultures for the *Streptococcus hemolyticus.*

Davis [17] states that there is no evidence to indicate that strains of streptococci pathogenic to man can even resist the usual temperature for pasteurization (145 F. for thirty minutes).

Reviewing the recent literature which is fairly well saturated with bacteriologic studies of the *Streptococcus hemolyticus,* one is impressed with the frequency which the organism inhabits the throats of not only persons suffering from acute infectious diseases, but the throats of normal persons (Otteraaen,[18] Smillie,[19] Pilot and Davis,[20] Havens and Taylor,[21] and Pilot and Pearlman [22]).

In fact, Davis [23] states that cultures taken at short intervals sooner or later reveal the presence of hemolytic streptococci in the throats of virtually all normal adult persons. True, they are found less frequently

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12. Irons and Marine: J. A. M. A. **70**:687 (March 9) 1918.
13. MacLennan and McNee: Brit. J. Dis. Child. **10**:258, 1913.
14. Davis: J. Infect. Dis. **23**:559, 1918.
15. Jones: J. Exper. M. **31**:347, 1920.
16. Salter: Am. J. Hyg. **1**:154, 1921.
17. Davis: Am. J. Pub. Health **8**:40, 1918.
18. Otteraaen: J. Infect. Dis. **26**:23, 1920.
19. Smillie: J. Infect. Dis. **20**:45, 1917.
20. Pilot and Davis: J. Infect. Dis. **24**:386, 1919.
21. Havens and Taylor: Am. J. Hyg. **1**:192, 1921.
22. Pilot and Pearlman: J. Infect. Dis. **29**:47, 1921.
23. Davis: J. Infect. Dis. **29**:524, 1921.

in the normal throat after tonsillectomy, as reported by Tongs,[24] Bryan,[25] Nichols and Bryan,[26] Van Dyke,[27] Pilot and Davis,[20] and Meyer, Pilot and Pearlman.[28]

However, Bloomfield,[29] reporting on the significance of bacteria found in the throats of healthy people, states that hemolytic streptococci of the typical beta type (pathogenic) were not obtained in any case.

This is of interest, as the cultures were made from people who were in intimate contact with patients suffering from sore throats due to these organisms. We believe that their presence in normal throats, as reported by some writers, indicates the recent presence of widespread infection among large groups of people with a virulent type of the germ.

These facts lead one to suspect that in the epidemic under study we were dealing with a different strain of hemolytic streptococcus than the ordinary throat inhabitant, or that the virulence of one of the streptococcus strains inhabiting the normal throat became activated and by contact infection (mainly hand infection, in the present case) was spread to other members of the ward.[30]

I wish to express my appreciation to Dr. Robert G. Hall for his courtesy in permitting me to study and report these cases, to Dr. R. L. Benson and Dr. F. R. Menne for the necropsy reports and for their study of the throat cultures of the adults, and to Huntley and Howe Laboratory for their cooperation in examining the blood cultures.

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24. Tongs: J. A. M. A. **73**:1050 (Oct. 4) 1919.
25. Bryan: Ann. Otol., Rhinol. & Laryngol. **28**:337, 1919.
26. Nichols and Bryan: J. A. M. A. **71**:1813, 1918.
27. Van Dyke: J. A. M. A. **74**:448 (Feb. 14) 1920.
28. Meyer, Pilot and Pearlman: J. Infect. Dis. **29**:59, 1921.
29. Bloomfield: Johns Hopkins Hosp. Bull. **32**:33, 1921.
30. At the present time (April 1922) Portland is having an epidemic of septic sore throat, undoubtedly due to contaminated milk. There have been several deaths among infants due to streptococci septicemia with terminal peritonitis.

BOOK REVIEW

HAUTKRANKHEITEN UND SYPHILIS IM SAUGLINGS UND KINDESALTER. An Atlas. PROFESSORS H. FINKELSTEIN, E. GALEWSKY and L. HALBERSTAEDTER. Berlin, Julius Springer, 1922.

The authors give a brief but comprehensive summary of most of the skin diseases seen during infancy and childhood. Wherever possible, their plan has been to give a description of the skin lesion, followed by a discussion of the symptomatology, the general course of the condition and a differential diagnosis. They add a few words on prognosis and conclude with an outline of the treatment, both general and local, not forgetting to mention prophylaxis. The most important feature for the average physician, however, is the inclusion of numerous colored plates. Each condition described has its accompanying illustration and thus the practitioner is enabled to form a visual conception of the lesion. While it is impossible to duplicate exactly the finer shades of color or the minute details of configuration, still the representations are sufficiently true to life to recall immediately the disease. This volume will prove a valuable addition to any pediatrician's library.

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THE HORSE SERUM (FOREIGN PROTEIN) TREATMENT OF PYELITIS AND PYURIA *

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Until recently we have been unable to determine definitely whether a given case of pyuria is one of pyelitis, cystitis, or pyelocystitis. Common custom has been to designate all cases presenting the more or less characteristic symptoms when associated with a definite excess of leukocytes in the uncentrifugated urine or definite pus in the sediment pyelitis. Particularly was this diagnosis considered very probable if the urine was acid and colon bacilli were found in smear and on culture. It is only possible, however, to diagnose pyelitis definitely by means of the cystoscope which enables one to differentiate the portion of the renovesical system from which the pus is coming. It is possible to demonstrate this by means of kidney massage and a certain technic which I described fifteen years ago,[1] but the cystoscopic method is by far the best method and instruments are now made small enough to pass into an infant's bladder and permit of ureteral catheterization.

Some clinicians have gone so far as to assert that unless the colon bacillus is found we are not dealing with a pyelitis. This opinion, however, is held now by but a few. A case recently observed in a young woman, aged 20, with pyuria of three years' standing illustrates this point very well. The urine was heavy with pus, the stained specimen showed pure culture of a coccus; specimen from the right ureter showed the same, and culture proved the coccus to be *Staphylococcus pyogenes albus*. The urine was at all times distinctly acid, which is not the rule with this type of infection. The *Staphylococcus albus* splits urea, rendering the urine alkaline, but it has failed to do so in this case and no organisms were associated with it that would ferment sugars. Case 8 also illustrates this point and it is interesting to note a double infection in this patient. The colon bacillus was recovered from the right ureter, the *Staphylococcus albus* from the left.

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* From the Department of Pediatrics and Infectious Diseases, University Hospital.

[1] Cowie: Am. Med. **11**:36, 1907.

Nor can we determine a pyelitis by the symptom of pain in the flank, below the costal margin or in the kidney region, even when it is associated with fever and pyuria. I have recently seen a case of pyuria in a woman, aged 56, with pain in the right kidney region, pyuria, colon bacillus on culture, and acid urine. On cystoscopic examination an infected bladder was found and clear urine from both ureters. There were no classical vesical symptoms in this case. Pyelograms showed the kidneys to be normal in shape, etc. These cases serve to show that symptoms characteristic of pyelitis, even distinct pain in the kidney region, may not be due to pyelitis; that pyelitis may definitely be present and the affected kidney deliver acid urine containing the *Staphylococcus albus*.

My experience deals with the treatment of a number of cases of pyuria, some of which are doubtless cases of pyelitis by the older standards, but only two of which have been proved to be pyelitis by cystoscopic examination. The cystoscopic examinations were made by Dr. Hugh Cabot.

A case (1) of pyuria of long standing in a girl, aged 10, came for treatment Jan. 21, 1916, while I was studying the effect of Bier's hyperemic stasis in arthritis. Having had difficulty in clearing up cases of pyelitis in infants and young children by the usual methods, it occurred to me that if we could induce a hyperemia of the kidneys an infected pelvis might be cured. It is a well known fact that horse serum brings about a hyperemia of the skin and joints and might induce a hyperemia of some of the internal organs. I decided to induce hyperallergy in this patient with horse serum, and then produce an immediate reaction at will with the idea that during the reaction the kidneys might become engorged with blood and a result similar to that which occurs in arthritis after hyperemic stasis be produced. I did this and was interested to find that the pus disappeared from the urine completely after the third subcutaneous injection with no recurrence to the present time.

However, I am not at all convinced that my reasoning as to the explanation for this is correct. Since this time, much knowledge has accumulated on the action of foreign protein in infectious processes in general. The bulk of evidence would appear to support the idea that the beneficial effects obtained in treating pyuria with horse serum come from the nonspecific action of the protein itself, which we think mobilizes the normal antibodies of the circulating fluids to the affected part. There seems to be some evidence that this is associated with the production of blood engorgement, as is evidenced by increased temperature in affected joints during a protein paroxysm. However, we are by no means out of the realm of theory at the present time.

It must be quite evident that there is a difference between the action of the various protein substances used in the treatment of infections. We have found that the intravenous injection of dead typhoid bacilli and colon bacilli produced no effect in a few cases of pyuria which responded to subsequent treatment with horse serum given subcutaneously. There is a difference in the reaction induced by the various foreign proteins. (Case 5 illustrates this point.) There is no question in my mind that the protein of dead typhoid bacilli is the best protein to use for many of the infections. Bacterial proteins, particularly this one, give a marked reaction whether given intravenously or subcutaneously. Milk, in the few cases in which I have used it, may give little or no reaction subcutaneously. Horse serum intravenously, as we have recorded elsewhere,[2] induces reactions analogous to, if not identical with, those of dead typhoid bacilli. Subcutaneously, it also induces a similar reaction. In our experience it may stop or ameloriate an attack of whooping cough, an attack of acute cervical adenitis (glandular fever) and cause a subsidence of the glandular swellings. But for some reason it has appeared to cure a case of pyuria when the bacterial protein has failed to do so (Case 5).

Kempton,[3] Greenthal[4] and myself have shown that horse serum protects a guinea-pig against several fatal doses of diphtheria toxin when administered to the pig subcutaneously. Greenthal and I have, we think, quite definitely shown that this effect of the horse serum is due to a substance aside from the protein that neutralizes, or antagonizes, the action of the toxin. The albumin, or the globulin of horse serum freed from this substance, has no effect in preventing the fatal effect of diphtheria toxin. The globulin must be attached to this antisubstance before it can be effective. We are unable to separate the anti-substance from the globulin. Now, diphtheria antitoxin, when administered in these infections, acts in the same way. Hence we are at a loss to say whether pyelitis or pyuria is benefited by the protein of the horse serum or the combination of protein with antisubstance. Evidently the effect does not depend on hyperemia as a result of hyperallergy, for in other cases we have seen that beneficial effects sometimes come with the first injection, ahead of the development of the symptoms of serum disease. Hyperemia may occur under this condition.

We have several cases in which long controls with other methods aid us in making the statement that horse serum very often clears up a refractory case. I will cite another example.

Ann E. (Case 2), aged 1 year, presented the symptoms of attacks of high fever and gastro-intestinal upsets. Physical examination was negative, except for the finding of pus in an acid urine and the presence of colon bacilli. The case was treated by the usual methods for several months, but the attacks continued to recur. It was hoped the case would recover without the necessity of sensitizing the child to horse serum. This proved to be unsound reasoning, as a pyelitis might be quite as serious a disease as the ordinary case of diphtheria for which we would not hesitate to give a dose of antitoxin. At my request Dr. Kempton gave a dose of 3 c.c. of horse serum subcutaneously. This ended the condition. In the course of two or three days the pus had disappeared from the urine and has not returned to date (now over 3 years).

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[2] Cowie and Calhoun: Arch. Int. Med. **23**:131 (Jan.) 1919.

[3] Cowie and Kempton: J. M. Research **42**:227, 1921.

[4] Cowie and Greenthal: J. M. Research **42**:261, 1921.

On the other hand, and this seems a strange coincidence, an adopted sister of this little patient (Case 3), a girl, aged 3 years, developed the same symptoms about two years later (attacks of high fever) but in a more aggravated form, which have persisted off and on for more than nine months. Many horse serum injections have been given without the slightest effect in clearing up the pus which is visible to the unaided eye, and which has been proved by Dr. Cabot to be coming from the right kidney. This examination showed that the bladder walls were clear, the orifice to the left ureter patent, the orifice to the right pouting, and the passage of the catheter into the ureter obstructed one-eighth inch above the bladder, while the catheter passed readily into the left kidney, from whence clear urine proceeded to flow.

I am reporting these experiments, not with the idea of advocating the general adoption of this method of treating pyogenic infections of the genito-urinary apparatus, but from the standpoint of interest in developing a knowledge of the action of nonspecific foreign protein in disease process. I am definitely opposed to the indiscriminate injection of alien substances into the body. They may eventually prove to be absolutely noninjurious but at the present time we certainly know too little about the ultimate results of the injection of so many substances—pollens, vaccines, vegetable and animal proteins of various kinds, as well as of carbohydrates and salts. The point we wish to clear is whether the unquestioned cure in a few cases is due to the protein, the antisubstance, or the combination of protein and antisubstance.

REPORT OF CASES

CASE 1 (No. 4-3427).—Sarah R., aged 9 years, entered April 9, 1917, complaining of sharp cutting pains in right side and fever. Pus in the urine was treated with hexamethylenamin without relieving the condition. There was definite response to horse serum injections, as noted by distinct clearing up of the urine. Patient left the hospital before the urine was perfectly clear.

Comment.—The only value this case affords is the fact that following the horse serum injections there was definite improvement while previous treatment had brought about no change. It is well known, however, that pyelitis, untreated, may clear up to reappear again after a number of days.

Case 2 (No. 5-2676).—Walter N., aged 3½ years, entered the hospital, Aug. 15, 1917, for chronic nephritis and dermatitis exfoliativa. This patient also had a marked pyuria, colon infection.

The diagnosis was pyelonephritis.

He had been treated by the alternate alkaline and acid method and hexamethylenamin over a long period. Two injections of horse serum of 3 c.c. each cleared the skin up quite promptly but not permanently. No effect on the pyuria was secured from the horse serum treatment in this case.

Case 3 (No. 6-4679).—Mary McG., aged 9 months, entered the hospital, March 23, 1919, for failure to gain weight, pyuria, colon bacilli. Acid and alkaline treatment was employed until April 26 when she was given 200 million dead typhoid bacilli intravenously. April 30 another similar dose was given. No improvement followed. May 19, she was given 5 c.c. horse serum subcutaneously. Symptoms of serum sickness developed. Patient was discharged May 24. The pus cleared slowly but a slight temperature elevation persisted. She returned June 1, having gained 12 ounces in weight. She was taking food normally and made no further complaints concerning the pyuria.

Case 4 (No. 7-4941).—Zona M., aged 5 years, entered the hospital, Oct. 23, 1919, with frequent urination, thirst, following an attack of mumps, pain and tenderness in the back at the site of the right kidney, and fever from 103 to 105 F., during the last four days. She was admitted as an emergency case. A catheterized specimen of urine was acid and contained albumin and pus. Physical examination was negative.

November 17: Patient had been treated by forcing fluids. There was a definite improvement, as recognized by a subsidence of the fever, gain in weight and the development of a good appetite. The pus in the urine was lessened but still quite marked. Four cubic centimeters of horse serum was given subcutaneously. No reaction following this injection.

November 25: Albumin, faint; few pus cells.

December 2: Albumin negative, few pus cells; 2 c.c. of horse serum given subcutaneously.

December 4: Few pus cells; 4 c.c. horse serum given subcutaneously.

December 11: Few pus cells. Patient developed measles.

Jan. 6, 1920: Catheterized specimen of urine shows only an occasional leukocyte. Colon bacilli, positive.

January 7: Two leukocytes in ten fields.

January 8: Only occasional leukocytes.

January 17: No leukocytes found.

Comment.—It will be noted in this case that the greater improvement occurred after the patient had had measles, although prior to that time there was no question as to the reduction in the number of leukocytes.

Case 5 (No. 8-4863).—Robert C., aged 8 years, entered the hospital Sept. 5, 1919, with remittent fever, marked pyuria and colon infection. Alkaline-acid treatment was not followed by improvement.

November 11: Horse serum, 5 c.c.

November 18: Tonsillectomy.

November 20: Serum reaction from horse serum.

December 2: Reaction subsided; 2.5 c.c. horse serum.

December 4: Five cubic centimeters horse serum. A slight excess of leukocytes in the centrifugated sediment.

After the first horse serum there was improvement in the amount of pus. Tonsils were removed soon after this and pus reappeared in the urine. On discharge there were a few cells found in the sediment. Marked improvement. Discharged Dec. 18, 1919.

Case 6 (No. 9-5202).—Gale W., aged 9 years, entered the hospital, April 9, 1920, with pain in right hip joint, delirium, fever, 103 F., nosebleed, pus in urine. Sudden onset four months ago (January 15). Pain began in right hip over trochanter major requiring morphin; pain on motion of the right leg. This continued more or less for a week when fever developed, with delirium and nosebleed.

Cystoscopic examination showed pus from both ureters. Urine from right kidney showed colon bacillus; urine from the left kidney *Staphylococcus albus.*

Alkaline-acid treatment, hexamethylenamin, then back to acid-alkaline treatment. No improvement was secured. The urine sediment showed *Staphylococcus albus.*

May 25: Leukocytes, 12,000. Pus continues in the urine. Five cubic centimeters horse serum subcutaneously.

May 27: Urine is still cloudy, thick mucus-like sediment containing much pus; settling out after twelve hours in the test tube shows one third by volume. Five cubic centimeters horse serum subcutaneously.

June 6: Marked symptoms of serum sickness.

June 8: Serum reaction continues; temperature 103 F.; pain in joints; marked itching.

June 10: Serum reaction subsided; considerable mucus but no pus cells found in urine, fourteen days after last horse serum.

June 14: Discharged apparently well; urine entirely negative.

June 24: Doctor writes pus again in urine. This was diagnosed macroscopically.

Comment.—In this case there was immediate effect from the horse serum but apparently it was not permanent. We have not been able to get any further urine samples.

Case 7 (No. 10-6563).—Ellen S., aged 1 year, entered hospital, Jan. 10, 1921. Diagnosis: Pyelonephritis.

Three injections of horse serum. Definite improvement but not permanent. The baby also had marked eczema and cervical adenitis. This condition was apparently cured by the horse serum.

Case 8 (No. 11-5529).—Evangeline P., aged 7 years, entered hospital, Oct. 1, 1920, with chills, fever up to 105 F., diarrhea of six weeks' duration; no pain. Physical examination negative, except pulse, 120; temperature, 102 F.; systolic murmur at the apex and aortic area; no thrills; all of which disappeared after a few days in the hospital, no cardiac enlargement.

Urine: Acid; albumin, positive; pus, marked.

October 4: Fever, 102 F. Catheterized specimen for culture contained pus. Hexamethylenamin, 10 grains, four times daily.

October 9: No improvement. Culture shows colon infection. Hexamethylenamin stopped. Salol treatment begun.

October 12: Pus continues; no change.

October 13: Pus continues; no change. Salol stopped; 5 c.c. horse serum subcutaneously.

October 14: Pus the same.

October 15: Pus the same.

October 18: Pus the same.

October 20: Pus the same.

October 29: Pus the same.

November 2: Pus the same.

There has been no reaction from the horse serum (5 c.c. subcutaneously).

November 4: Pus the same, no change.

November 6: Five c.c. horse serum, subcutaneously.

November 10: Pus is very much less in amount.

November 15: There has been practically no pus since November 10. Temperature normal for two weeks.

November 17: Five c.c. horse serum.

November 18: Only a few leukocytes. Catheterized specimen. Culture examined twelve and thirty-six hours, and three days later. No fermentation, no motile bacilli present.

Colon infection has apparently completely cleared up.

Case 9 (No. 12).—A girl, aged 17, observed by Dr. Kempton, gave a history of eight or ten attacks of chills, high temperature, and abdominal pain over a period of two years. Examination of the urine during the last attack showed abundance of pus and colon bacilli.

Following intramuscular injection of 10 c.c. of horse serum, the temperature fell to normal the following day and remained normal. The urine, however, continued to show considerable amounts of pus until after a very severe attack of serum disease which occurred on the ninth day. Following the attack of urticaria, four examinations of the sediment showed only occasional pus cells. Laboratory records show a temporary decrease in the amount of pus the day following the injection. Eight months have now elapsed with no recurrence of symptoms of pyelitis.

July 19, 1921: Leukocytes, 11,500; pus, four plus; colon bacilli.
July 26: Pus, two plus.
August 12: Pus, three plus.
August 13: Intramuscular injection of 10 c.c. horse serum.
August 14: Improvement; normal temperature; pus, minus.
August 15: Pus, two plus.
August 16: Pus, two plus.
August 19: Macroscopic pus; not examined.
August 22: Serum disease.
August 24: Only occasional leukocyte.
August 25: Only occasional leukocyte.
September 8: Only occasional leukocyte.
September 15: Only occasional leukocyte.[5]

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[5] Personal communication.

DYSKERATOSIS DIFFUSA CONGENITA *

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AMSTERDAM

REPORT OF CASE

History.—The infant was born normally at term. It cried directly after birth and the meconium and urine were evacuated before the child had anything by mouth. It is the first child of healthy parents. There is no history of miscarriages or of tuberculosis.

Examination.—When 1 day old the baby was examined and it was noted that the skin had a yellow brown color and resembled parchment. The epidermis was for the greater part detached from the underlying layers. There was no sign of trauma except in the groins, which showed some excoriation, and where the underlying stratum was traumatized, the corium was laid bare.

There was much secretion from the vagina. The face was quite devoid of expression and resembled a plaster cast. The eyelids of both eyes showed signs of ectropion. The conjunctiva was of a bright red color. The mouth was very large and always open like the mouth of a fish. The somewhat ectropied lips showed radial fissures. Nothing special was noted inside the mouth.

As far as could be ascertained, the chest and abdomen were negative. Neither the palms of the hands nor the soles of the feet showed any sign of pemphigus. The hair was normal, the ears were well shaped, although their outlines seemed a little vague on account of the peculiarities of the skin.

The patient was brought to the hospital on the evening of the same day, when the following was noted. The child drank and cried normally. The skin was torn here and there and was beginning to come off in big patches. The underlayer of epidermis was somewhat reddened, but appeared to be normal except for some fissures extending down to the corium. Later on the shedding of the skin increased, extending over the trunk, the head and the extremities.

Aug. 28, 1921: General condition was not unfavorable. The shedding of the skin continued.

August 24: Large patches of skin hung loosely from the trunk, arms and legs. The light red underlayer generally appeared to be normal, except for some fissures here and there.

The patient became restless and showed attacks of tremor of considerable amplitude (especially in the arms), which subsequently extended over the entire body.

Examination of the Blood.—Hemoglobin (Sahli), 123 per cent.; red cells, 8,360,000; white cells, 11,000; polymorphonuclear neutrophils, 30 per cent.; eosinophils, 0.3 per cent.; basophils, 1 per cent.; lymphocytes, 48.3 per cent.; transitionals, 8 per cent.; myelocytes, 11.8 per cent.; Türk's forms, 0.6 per cent. When making the differential count of 350 white cells, ninety-three normoblasts and two megaloblasts were seen. The chromocytes were well shaped. There were some megalocytes. Metachromasia was apparent. Large lymphocytes were strikingly few in number; the majority of the lymphocytes being of the smaller type with little protoplasma, the blood platelets were for the greater part of a large size.

Course.—Death occurred in the evening.

EXAMINATION OF SKIN

A complete postmortem examination was not permitted, so we could only examine the skin of the back and of the chest. The stratum

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* Received for publication, May 20, 1922.

* From the Hospital for Sick Children.

corneum in some places was of normal thickness, whereas in other places it was either thicker or thinner. The border of the horny layer was irregular. The stratum corneum and the stratum granulosum could be differentiated. It is remarkable that all over the stratum corneum, even in its most peripheral parts, here and there nuclei were found, some of which stained easily with hematoxylin, whereas others did not stain at all. Normally, this layer has no nuclei. In other preparations the stratum corneum has a perfectly normal appearance and, again, in still others it looks like a coagulated mass—the product of combustion without the charred surface.

The stratum granulosum is nowhere well developed and the quantity of keratohyaline substance is doubtless less than in normal cases

The structure of the rete Malpighii is irregular. The papillae are of various sizes, some of them being very large. The papillae do not run parallel to each other, but in different directions. The epithelium is irregular and unequal. There is no edema worth mentioning. The thickness of the epidermis varies considerably in different places. There are no symptoms of inflammation, although the blood vessels are very full, which, however, is a physiologic characteristic of this age. Neither the sweat glands nor the sebaceous glands show any abnormality. Thus, in this case, it is not a question of hyperkeratosis but of dyskeratosis diffusa congenita. The abnormal stratum corneum cannot prevent the skin from drying in.

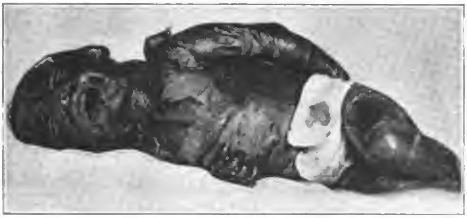

Fig. 1.—Large patches of skin are seen to hang loosely from the chest and shoulders.

An examination of Figures 1 and 2 leaves no room for doubt that the case is one of ichthyosis congenita, or, strictly speaking, keratoma diffusum universale congenitum (Kyber), the term ichthyosis being erroneously, and too often, applied to this disease. Indeed, the descriptions of cases published by different authors present such a striking resemblance that, as one of these authors humorously remarked, every one of them might have committed plagiarism of the same case, without being detected.

The first description (by Richter) of this rather rarely appearing cutaneous disease dates back to 1792, and since then the subject has never ceased to interest medical authors. In 1921 two extensive articles appeared, one by Golay [1] and one by Hess and Schultz,[2] besides a short report by McAustin.[3] In 1849, this disease was discovered by G. Vrolk.[4] Both he and Müller were the first to make histologic preparations. The extensive literature on the subject can be found in the articles of Ballantyne,[5] Riecke,[6] Fulci,[7] Golay,[1] Hess and Schultz.[2] As there is no reason for repeating their reports, we will only point out the histologic difference between our case and the majority of other cases that have hitherto been described.

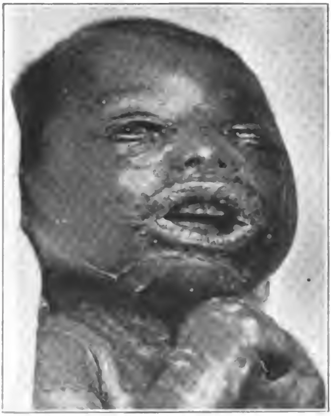

Fig. 2.—The face resembles a plaster cast. The mouth is fixed in fishlike position.

Most of these cases are very serious ones and are classified by Riecke as ichthyosis congenita katexochen. The majority of these infants are prematurely born, if they are not stillborn. The retraction of the skin causes deformity of the hands and feet. As to the ears and nose, often only the apertures of these structures are to be seen. The skin is fissured all over from birth. In a second group, called by Riecke ichthyosis congenita larvata, various symptoms are less or only partly apparent. Instead of "larvata" we would rather use the term "mitior." In Riecke's third group (ichthyosis congenita tarda) scarcely any symptoms or none at all are to be detected at birth. Still they do appear sooner or later, after days or weeks or months, ultimately presenting the aspect of the second group. After vegetating a little while, these patients generally die of some intercurrent illness.

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[1] Golay: Ann. de dermat. et de syph. **2**: No. 3, 1921.

[2] Hess and Schultz: Am. J. Dis. Child. **21**:357 (April) 1921.

[3] McAustin: Brit. M. J. **1**:155 (Jan. 29) 1921.

[4] Vrolyk, G.: Concerning a Singular Defect of the Skin Observed in a First Infant, Amsterdam, 1849.

[5] Ballantyne: Manual of Antenatal Pathology and Hygiene, The Fetus, 1902.

[6] Riecke: Arch. f. dermat. u. Syph. **54**:289, 1900.

[7] Fulci: Arch. de méd. exper. et d'anat. path. **22**:1.

In many respects our case seems to correspond to Ballantyne's description of ichthyosis congenitor mitior.[8] According to him this group is formed by infants whose skin at birth has no fissures and looks like parchment or collodium (it has been rightly compared by Hess and Schultz to the peal of a puffed apple). Fissures appear later. The limbs of our patient were not deformed. Moreover, the infant was fullgrown and it did not die before the fourth day.

In all cases which have been described previously, the thickness of the stratum corneum on microscopic examination was found to exceed ± 200 times that of normal skin. The extremely strong hornification of the hair-funnels seems to be another characteristic. Moreover, the lack of a stratum granulosum is mentioned by various authors. Fulci was not able to confirm this statement, the stratum lucidum being indistinct. Meyenburg,[9] on finding keratohyalin instead of eleidin in the stratum lucidum, concludes that there must be an extremely rapid transformation from the stratum malpighii to the stratum corneum. Carbone proved the rete malpighii to be hypertrophic. In the case described by Hess and Schultz both the stratum lucidum and the stratum granulare were missing. They explain the condition of the skin by the following theory: Primarily the skin must have been hypertrophic and provided with large papillae, which produced a great number of cells, thus forming a thick stratum corneum. The hypertrophic state is followed by atrophy, except in the horny layer. The papillae grow shorter and flatter and their interstices larger. Hairs, sweat glands and sebaceous glands disappear, whereas the elastic tissue diminishes. Secondary to these atrophic symptoms, the epidermis is fissured and the limbs are deformed as a result of the retraction of the skin. Contrary to this theory many authors reported that the glandular system and hairs were normal. According to Golay, hyperkeratosis is in the class of the "desquamation lamelleuse des nouveau-nés" and Brock's érythrodermie ichthyosiforme. He inclines to Bowen's theory of the subsistence of the epitrichium. Unna[10] clearly explains why it is not allowed in this respect to speak of ichthyosis. In cases of hyperkeratosis, contrary to ichthyosis, the stratum corneum is not only thickened, but also abnormally unelastic and, therefore, insufficient to cover the whole body. This causes retraction and ectropion, which symptoms are not known to occur even in the severest cases of ichthyosis. Ichthyosis generally appears on the extensor surface, rarely on the flexor surface, the face or the neck, and never on the palmar and plantar surfaces. In hyperkeratosis these peculiarities are absent, the disease is a diffuse one. Moreover, keratosis is a congenital disease and ichthyosis is not; the former is familial and the latter hereditary.

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[8] The term keratosis or keratoma should be substituted for ichthyosis congenita.

[9] Meyenburg: Diss., Berlin, 1912.

With our case of dyskeratosis we stand isolated from the majority of authors who describe the thick horny layer. However, the figure, borrowed by Ballantyne from an article by Caspary,[11] shows a general thickening of all the layers of the epidermis without the stratum corneum being conspicuous in this respect. Caspary's patient was an infant, aged 18 months.

The etiology of this singular disease is unknown. Syphilis seems to be out of the question, but the fact that the parents were related to each other may be an etiologic factor. The disease has been likened to anomalies of the organs of internal secretion, but the results obtained by microscopic examinations of the thymus, the thyroid and the suprarenals are not convincing. The information given by Golay is by far the most interesting. The first, second, fifth and seventh child of a certain woman showed symptoms of keratosis, whereas the other children were normal. During her pregnancy this woman had a great longing for salt. When she was able to resist this desire, her babies were normal. When, on the contrary, she indulged freely in the use of salt, the infants were born with the peculiar skin described above. This was confirmed by her husband. We are not informed of the quantity of salt she took. Golay does not feel inclined to reject, a priori, this etiology, salt being absorbed by the aminotic fluid, which he asserts, alters the normal osmotic relation. Moreover, salt has an unfavorable influence on the kidneys of the mother.

Finally, we want to speak of the peculiarities of the blood in our case. Most new-born children are known to have an increased number of red blood cells and a high hemoglobin percentage, whereas their blood contains some myelocytes and some normoblasts, but in our case these findings were far more pronounced. Golay is the only author who, in describing this disease, gave an account of the condition of the blood. Except for many large mononuclears, he did not find any abnormalities. In some cases of hyperkeratosis, as in severe burns,

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10. Unna: Die Histopathologie der Hautkrankheiten.

11. Caspary: Vierteljahrschr. f. Dermat. **13**:3, 1886, quoted by Ballantyne.

a congestion of the internal organs has been reported. Therefore, we searched the case histories of extensive burns, hoping to find there, in the condition of the blood, some analogy with our own case. That our researches were fruitless may easily be understood. In attending a case of extensive skin burn, the physician will, of course, concentrate his attention on the wound and abstain from unnecessary and painful examinations. Thus we are unable to give an explanation of the singular condition of the blood of our patient.

THE THYMIC SHADOW IN INFANTS*

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Reports on this subject have been made in recent medical literature, but the number of systematic investigations have been few, therefore it was thought that a study of the thymic shadow in infants, made at definite periods of their lives, and over a prescribed time, would offer material worthy of report.

For this purpose, a total of 119 new-born infants were examined roentgenologically. The first roentgenogram was made within forty-eight hours after birth; the second, ten days later, and then monthly thereafter, up to the end of the first year of life. Owing to the difficulties which are perfectly apparent, it was not possible to follow up many of these infants after the first month in the manner planned. For various reasons, many failed to return for subsequent examinations and were lost track of entirely. The material at our disposal, however, seems of sufficient interest to warrant this report.

In making the roentgenograms, the following technic was observed: The target-plate distance was 19 inches; spark-gap, 3 inches; milleamperage, 50, and the time of exposure, $\frac{1}{10}$ of a second. Films and double screens were used. Since it is well known (Gerstenberger) that the size of the so-called thymic shadow varies with the respiratory phase, it was attempted to make exposures at the end of full inspiration. Inasmuch as there is considerable discussion in the literature as to what constitutes a thymic shadow, and as to which mediastinal shadows may be due to normal structures alone, it seemed advisable to have some means of checking interpretations. The object of this was to determine two things. First, whether an upper mediastinal shadow, of the type usually interpreted as thymus gland, was obtained in the absence of a thymus, and second, whether the roentgen ray always demonstrates the presence of a thymus gland.

In pursuance of this, a total of fifty-five children were examined with the roentgen ray before postmortem, and the results compared with the actual findings at necropsy. The ages of the subjects ranged from 2 days to 10 years. In some older children, differentiation could be made only with difficulty of that part of the shadow due to the thymus,

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* From the Pediatrics Division of the New York Nursery and Child's Hospital and Department of Pediatrics of Cornell University Medical College.

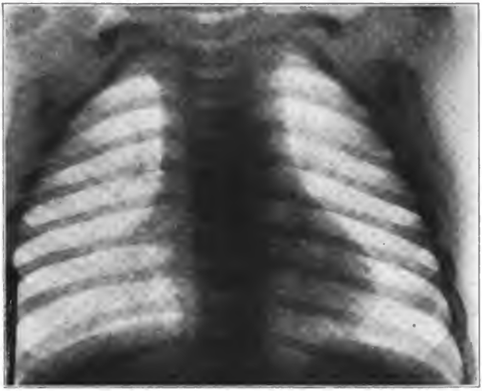

Fig. 1.—Columnar type thymus.

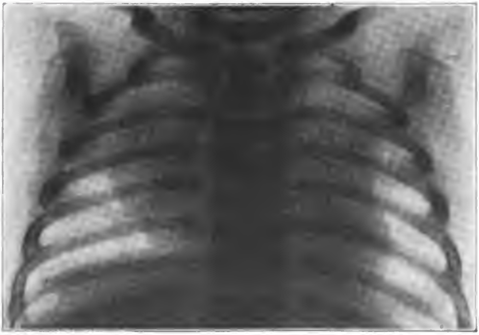

Fig. 2.—Bulbous type thymus.

from that due to other structures, such as glands and blood vessels; and at times this differentiation was impossible.

In thirty-six of the fifty-five postmortem cases, both actual and plate measurements were made for comparison. In twenty-one of the thirty-six cases, the difference lay between 0.5 cm. either way. In seven cases the difference lay between 0.5 and 1 cm., and in eight of the thirty-six it was more than 1 cm. For nonteleoroentgenograms, this was no great discrepancy. In two instances of the original fifty-five cases, there was no suggestion of thymic shadow, yet at the necropsy this condition was found, but in both these cases, the thymus overlay the heart, and was pedicle in type.

The thymic shadows found may be classified into three general types: (1) Columnar; (2) bulbous, and (3) pedicle, all of which are illustrated in the roentgenograms. The pedicled type is eliminated from work on the living, for it is one of difficult differentiation from heart shadow, into which it merges, and can, therefore, be discovered only at necropsy.

For work with the original 119 infants, the findings were divided into three classes:

Class 1. *Absent Thymic Shadow.*—This means no shadow apparent in the upper mediastinum, beyond the vertebral transverse processes.

Class 2. *A Small Thymic Shadow.*—This was found beyond the vertebral transverse processes, and measured less than 3 cm.

Class 3. *A Large Thymic Shadow.*—This shadow measured more than 3 cm. transversely.

This classification was applied at birth, and used throughout investigation. These are absolute terms, used as a working basis. A small thymus may yet be a large one in a chest with small transverse measurements, and conversely, a large thymic shadow may seem small in a large chest. This distinction is important when the question of treatment arises because of size alone.

RESULTS OF EXAMINATIONS

First examination (within forty-eight hours after birth):

Class 1—Absent thymic shadow, 35 cases
Class 2—Small thymic shadow, 34 cases
Class 3—Large thymic shadow, 50 cases

Therefore, at birth, approximately 42 per cent. of the children examined showed thymic shadows measuring more than 3 cm.; that is, shadows which we would read as thymus enlargement and regard as pathologic.

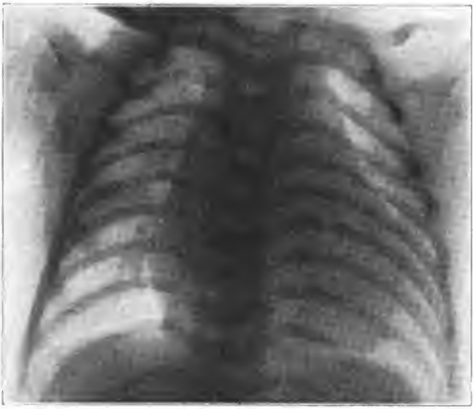

Fig. 3.—Pedicle type thymus.

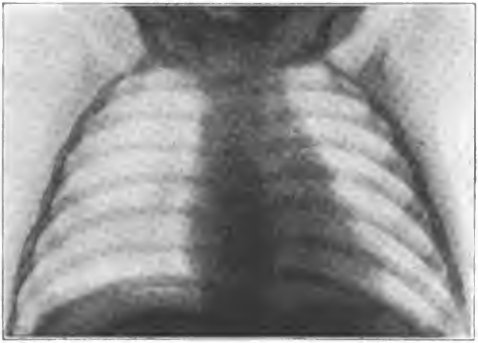

Fig. 4.—Class 1. Absent thymic shadow.

At the end of the first month of life, seventy-three of the original group of 119 children reported for reexamination. Of these, thirty-three were in Class 1; twenty-four in Class 2. Three of these Class 2 glands had definitely decreased in size. Sixteen were in Class 3. One of these glands had decreased in size.

Of a total of forty cases showing thymic shadow, small and large, four had undergone retrogression to smaller dimensions within the period of one month. This was a spontaneous change, for the single roentgen-ray exposure could be eliminated as a causative factor. Of forty-six children, the findings were:

- End of Second Month of Life:
  - Class 1—15 cases
  - Class 2— 6 cases (one had grown smaller)
  - Class 3—25 cases (no decrease in size)
- Third Month of Life, 39 Children:
  - Class 1—13 cases
  - Class 2— 4 cases (no decrease in size)
  - Class 3—22 cases (no decrease in size)
- Fourth Month of Life, 38 Children:
  - Class 1—13 cases
  - Class 2— 4 cases (no decrease in size)
  - Class 3—21 cases (two had decreased in size)
- Fifth Month of Life, 31 Children:
  - Class 1— 8 cases
  - Class 2— 4 cases (no decrease in size)
  - Class 3—19 cases (no decrease in size)
- Sixth Month of Life, 30 Children:
  - Class 1— 8 cases
  - Class 2— 4 cases (in one the thymus was confused by glands)
  - Class 3—18 cases (no decrease in size)
- Seventh Month of Life. 28 Children:
  - Class 1— 8 cases
  - Class 2— 2 cases (no decrease in size)
  - Class 3—18 cases (no decrease in size)
- Eighth Month of Life, 25 Children:
  - Class 1— 7 cases
  - Class 2— 2 cases (no decrease in size)
  - Class 3—16 cases (one had decreased in size)
- Ninth Month of Life, 22 Children:
  - Class 1— 6 cases
  - Class 2— 2 cases
  - Class 3—14 cases (no decrease in size)
- Tenth Month of Life, 17 Children:
  - Class 1— 5 cases
  - Class 2— 2 cases (no decrease in size)
  - Class 3—10 cases (one had decreased in size)

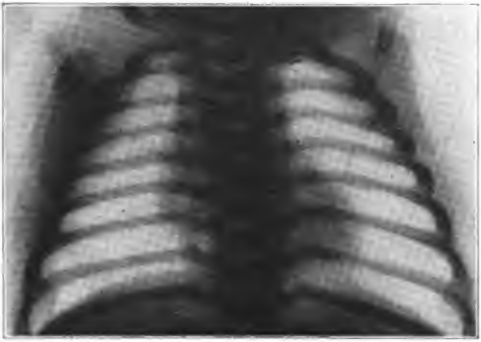

Fig. 5.—Class 2. Small thymic shadow.

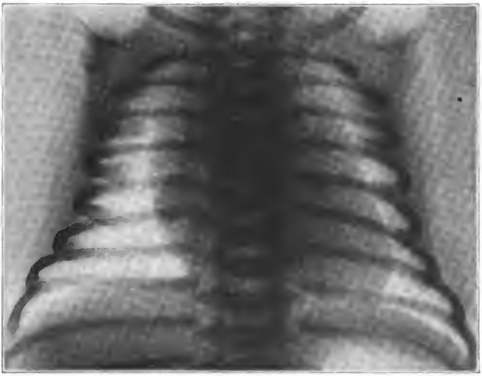

Fig. 6.—Class 3. Large thymic shadow.

ELEVENTH MONTH OF LIFE, 11 CHILDREN:
- Class 1—4 cases
- Class 2—2 cases (one had decreased in size)
- Class 3—5 cases (one was confused with gland shadow)

TWELFTH MONTH OF LIFE, 6 CHILDREN:
- Class 1—1 case
- Class 2—1 case
- Class 3—4 cases (one had decreased in size, and one assumed the shape of the pedicled type)

Some of the Class 1 cases were not reexamined after two successive examinations had shown no change. There were two known deaths in the original group of 119. The first was that of an infant assigned to Class 1, and the second of an infant in Class 3. At necropsy the findings confirmed the classification in both instances. The thymus of the second infant weighed 13 gm.

DISCUSSION

The striking revelation in this study was the fact that in a group of average "normal" infants at birth, 42 per cent. showed the presence of a shadow suggesting a thymus measuring more than 3 cm., and this without gross symptoms. As the work progressed, retrogression in size of the shadow took place, the greatest change within the first few months, a steady change as the year went by, so that with our limited material spontaneous disappearance of this shadow took place in the majority of cases. Some, however, persisted to the second year.

As a rule, the children with large thymic shadows were well nourished, some were large chested, with thick and short neck, and without physical stigmata. The general impression was, that the larger thymic shadows were present in the thick and short necked infants.

CONCLUSIONS

1. Thymic shadows can easily be determined in the new-born and in infancy.

2. Transversely, enlarged shadows are present in a strikingly high percentage of new-borns.

3. This shadow may be present without symptoms or physical stigmata.

4. There is a definite tendency for a spontaneous retrogression of this structure during the first year, but some glands persist beyond this period.

5. There is a type of thymic shadow cast by a pedicle-shaped organ, the mass of which lies on the heart, from which it cannot be differentiated.

6. In the later months of infancy, the presence of large paratracheal glands and prominent blood vessels presents some difficulty in differential diagnosis, but differentiation is possible.

I wish to acknowledge my indebtedness to the Obstetrics and Social Service Departments of the New York Nursery and Child's Hospital for their kind cooperation.

THE INORGANIC PHOSPHATE CONTENT OF BREAST MILK OF MOTHERS WITH NORMAL AND WITH RACHITIC INFANTS *

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The rôle of the phosphorus ion in the metabolism of rickets has recently acquired a prominence which is certain to be of the greatest moment. Clinically, we have learned form the work of Howland and Kramer [1] that infantile rickets, when active, is invariably accompanied by a reduction in the serum inorganic phosphorus and, as shown by Hess and Gutman,[2] this constituent of the blood rises as the rickets heals. Experimentally, the almost simultaneous and quite independent observations of Sherman and Pappenheimer [3] and of McCollum and his associates [4] have shown that rickets can be produced at will in the rat by a diet deficient in inorganic phosphorus, and that if this salt be added to the dietary in sufficient quantity, rickets fails to develop. However striking and conclusive these experimental observations may be, it is at once apparent that in the light of clinical experience they cannot indicate that infantile rickets is merely dependent on a deficient phosphorus supply. We know that cow's milk contains approximately five times as much phosphorus as woman's milk and yet we see rickets far more frequently among bottle fed babies. The question of the factors influencing the availability of an adequate supply we cannot discuss in the present state of our knowledge.

It was in view of the aforementioned studies in rat rickets that an investigation of the inorganic phosphate of breast milk was undertaken. For this purpose samples of milk were obtained from mothers attending the Newly Born Outpatient Service of the Touro Infirmary and their infants, all of whom were exclusively breast fed, were examined for rickets clinically and in some instances by serum phosphorus determinations.

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* Received for publication, May 15, 1922.

1. Howland, J., and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

2. Hess, A. W., and Gutman, M. B.: The Cure of Rickets by Sunlight Accompanied by an Increase in the Inorganic Phosphate of the Blood, J. A. M. A. **78**:29 (Jan. 7) 1922.

3. Sherman, H. C., and Pappenheimer, A. M.: Experimental Rickets in Rats. I. A Diet Producing Rickets in White Rats, and Its Prevention by the Addition of an Inorganic Salt, J. Exper. M. **34**:189 (Aug.) 1921.

4. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: The Production of Rickets by Diets Low in Phosphorus and Fat Soluble A, J. Biol. Chem. **47**:507 (Aug.) 1921.

Methods.—The samples of milk were collected as follows: The infant was allowed to nurse one breast for from fifteen to twenty minutes, after which approximately ½ ounce of the strippings was milked by manual expression. An equal quantity was then obtained of the foremilk from the other breast and the two were mixed. Thus, milk from both breasts was obtained, having a fat content probably equal in quantity to that of the entire milk of one breast. The milk was kept in the refrigerator until analyzed, always within three or four hours after milking.

TABLE 1.—INORGANIC PHOSPHATE CONTENT OF MOTHER'S MILK AND BLOOD SERUM OF NONRACHITIC INFANTS

Date	Age	Milk Phosphate Mg. per 100 C.c.	Serum Phosphate Mg. per 100 C.c.
11/28/21	2 weeks	4.2	...
12/ 6/21	2 weeks	4.1	...
12/ 8/21	2 weeks	3.9	...
12/ 9/21	3 days	4.8	...
12/10/21	3 months	3.2	...
12/13/21	2 months	6.2	...
12/17/21	5 months	3.0	...
12/21/21	4 months	5.0	...
12/28/21	3 weeks	2.5	...
1/20/22	4 weeks	*	5.8
1/23/22	6 weeks	2.6	...
1/26/22	5 months	4.4	4.6
1/28/22	6 weeks	*	4.1
2/ 9/22	2 months	5.4	5.7
2/11/22	2 months	5.1	5.4
2/16/22	4 months	2.6	4.9
2/25/22	8 months	5.0	4.6
3/ 4/22	3 months	3.3	5.0
Average		4.08	5.0

* Resisted coagulation.

TABLE 2.—INORGANIC PHOSPHATE CONTENT OF MOTHER'S MILK AND BLOOD SERUM OF RACHITIC INFANTS

Date	Months	Rickets Clinically	Milk Phosphate, Mg. per 100 C.c.	Serum Phosphate, Mg. per 100 C.c.
12/ 3/21	11	+	4.3	...
12/15/21	11	+	4.6	...
12/ 8/21	6	+	3.7	...
1/ 3/22	2	+	4.0	...
1/19/22	4	++	5.4	2.2
1/24/22	5	++	5.4	3.0
1/24/22	4	++	4.5	2.7
2/ 2/22	4½	+	5.7	3.6
2/ 2/22	4	++	5.4	3.4
2/14/22	19	++	*	2.5
3/18/22	8	+++	5.1	2.2
2/16/22†	4	±	2.7	4.1
Average			4.8	2.8

* Resisted coagulation. † Excluded from average.

The blood was obtained by longitudinal sinus puncture and the serum used as soon as possible. No plasma determinations were made for it has recently been shown[5] that a very slight excess of citrate or oxalate added to the blood leads to anomalous results. The inorganic phosphate determinations in the serums and milks were carried out by the method of Bell and Doisy.[6] The concentration of the inorganic phosphates in human milk is such that this method can be used virtually without modification. The only change made in the technic was the addition of 2 parts of the 20 per cent. trichloracetic acid solution to 1 part of milk, instead of equal parts of each. This was done to insure as complete coagulation of the milk proteins as possible. Occasionally a milk was obtained which resisted coagulation and such had to be discarded. A 1 : 10 dilution was used, both for milk and serum, and the dilute standard which Bell and Diosy recommended for blood plasma (10 c.c. ≡ 0.5 mg. P.) was used for the milk determinations. The results are collected in Tables 1 and 2.

I have excluded from the average the last case in Table 2, in which the evidence of rickets was slight and the serum phosphate was 4.1 mg. My average for the milk phosphate is in excellent agreement with that of Denis,[7] who found in twenty-one samples of mature breast milk an average of 4 mg. inorganic phosphate per 100 c.c., with variations from 2.3 to 5.4 mg. Sixteen years ago Sikes[8] published his results of phosphorus determinations on 300 samples of human milk during the first thirteen days of lactation and obtained somewhat higher figures for his "nonproteid" phosphorus. His average is 7 mg. nonproteid phosphorus in 100 gm. of milk. Holt, Courtney and Fales[9] give as their average for mature milk 7.4 mg. phosphorus per 100 c.c.

SUMMARY

1. Inorganic phosphate determinations of serums of eight nonrachitic infants showed an average of 5 mg. per 100 c.c.

2. Sixteen samples of breast milk of mothers whose infants showed no evidence of rickets contained an average of 4 mg. inorganic phosphate per 100 c.c. milk.

3. The serums of seven rachitic infants were examined and the average value for the inorganic phosphate was 2.8 mg. per 100 c.c.

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[5] Denis, W., and von Meysenbug, L.: Note on a Possible Source of Error in the Bell-Doisy Method for Determination of Phosphates in Blood Plasma, J. Biol. Chem. **2**:1 (May) 1922.

[6] Bell, R. C., and Doisy, E. A.: Rapid Colorimetric Methods for the Determination of Phosphorus in Urine and Blood, J. Biol. Chem. **44**:55 (Oct.) 1920.

[7] Denis, W.: Unpublished work.

[8] Sikes, A. W.: On the Phosphorus and Calcium of Human Milk, J. Physiol. **34**:464 (Oct. 29) 1906.

[9] Holt, L. E.; Courtney, Angelia M., and Fales, Helen L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**:229 (Oct.) 1915.

4. The breast milk of mothers of rachitic infants was found to contain an average of 4.8 mg. inorganic phosphate per 100 c.c.—an average which falls within the "normal" range.

CONCLUSIONS

1. There is no reduction in the inorganic phosphate of the breast milk on which infants develop rickets.

2. The finding of other observers that the inorganic phosphate content of the serum is reduced in rickets is corroborated.

INDICATIONS FOR TONSILLECTOMY IN INFANCY AND CHILDHOOD. IS THE MODERN TENDENCY TOWARD UNIVERSAL TONSILLECTOMY JUSTIFIED?*

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During the past few years there has been engendered in the minds of medical men an unbounded spirit of antagonism toward the faucial tonsils. The pendulum has been swinging toward extreme radicalism. The tonsils have been held responsible for almost every disease of childhood. As portals of entry and foci of infection they have been accused of producing every form of pathologic condition. The obsession has spread to the laity who are now, with or without medical advice, demanding the complete removal of the tonsils as a routine hygienic measure.

Last year the medical school inspectors of New York City recommended tonsil treatment for 49,230 children. If the problem were extended to the whole country it would undoubtedly include more than a million children.

Tonsillectomy is quite a major operation. Its risks are very definite. Numerous serious complications have been reported. A large number have not been reported. The indiscriminate removal of the tonsils should be condemned.

I shall outline briefly the history of tonsillectomy, discuss the functions of the tonsils and present an analysis of 200 cases observed in private practice in which the tonsils had been removed for a variety of reasons. I shall endeavor to formulate rational indications for tonsillectomy.

The first account of the tonsil operation was given by Celsus in A. D. 10, who recommended removal of the tonsils if they "remain indurated after inflammation." Aetus, in A. D. 490, writes more conservatively of the excision of the tonsils. In A. D. 1120, Albucasis expressed his fear of hemorrhages after tonsil operations. During the next 500 years the operation was not done. It was revived in 1637 by Servius and criticized later by Dionus, who claimed that the tonsils had definite functions. Meseati and Wiseman were the first to employ it in modern times.

The functions of the tonsils have long been the subject of much study and experimental work, and a large mass of contradictory conclusions may be found in the literature. A careful sifting of the material and critical observation of cases, however, cannot but lead one to the conviction that the tonsils have definite functions to perform.

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* Read before the Thirty-Fourth Annual Meeting of the American Pediatric Society, held at Washington, D. C., May 1-3, 1922.

In our enthusiasm over tonsillectomy, these functions are frequently entirely discarded.

The anatomy of the organs shows that they are practically aggregations of lymph nodes covered by epithelium. Indentations occur forming the crypts.

Like other lymph nodes the tonsils exercise a protective function. They act as a sieve, the "first line of defense" against microbic invasion. Stöhr [1] has shown that the tonsils are traversed by an enormous number of leukocytes which exercise a kind of migration toward the surface.

The work of Adami and Nicholls [2] leads them to say:

> The tonsils appear to have an important function. While the lymphoid cells are themselves, to a limited degree, phagocytic, polymorphonuclear leukocytes in considerable numbers make their way from the blood vessels to the surface through the epithelial covering. These leukocytes are strongly phagocytic and their activity suggests that the tonsils form one of the barriers against the invasion of the system by pathogenic micro-organisms.

Henke [3] proved by numerous experiments that there was a constant lymph current passing from the mucous membrane of the nose and gums through the tonsil to its surface. This must undoubtedly act as a strong force in combating bacterial invasions. The reaction of the tonsil is commonly noted, while the original source of the infection, whether it be in the nose, the accessory sinuses, or in the mucous membrane of the mouth, is entirely disregarded.

The posterior pharyngeal wall, the postnasal space and the intestinal wall contain innumerable lymph follicles similar to those of the tonsil. If this type of structure was especially susceptible as a portal of entry or focus of infection, of what avail would be the removal of the tonsils?

Before antitoxin was introduced, it was common knowledge that diphtheria ran a milder course when localized to the tonsils than when it involved other parts.

Tonsillitis alone, or when associated with other conditions, is usually only a manifestation of systemic infection. If the infection becomes more generalized, it occurs in spite of the tonsil, not because of it.

In rare instances, however, the tonsils may cease to function and become "choked filters" in which cases they may be a source of infection. The diseased condition should be proved before the tonsils are sacrificed.

The rôle played by the tonsils in the production of lymphocytes has been conclusively demonstrated by Wood.[4] He regards this as a most important function. Piersol [5] showed that large numbers of lymphoid cells pass through the tonsils into the oral cavity to become the salivary corpuscles.

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1. Quoted by Comroe: J. A. M. A. **63**:1367 (Oct. 17) 1914.
2. Adami and Nicholls: Principles of Pathology **2**: p. 391.
3. Henke: Arch. f. Laryngol. **27**: Pt. 2, 1914.
4. Wood, G. B.: Univ. Penn. Med. Bull. (Oct.) 1904.
5. Quoted by Comroe: J. A. M. A. **63**:1368 (Oct. 17) 1914.

Masini[6] believed that the tonsils developed an internal secretion, similar to the suprarenal gland, but this has not been substantiated by sufficient evidence.

The tonsils have an important part to take in the lubrication of the food as well as of the throat during the act of speaking and singing. I have frequently noted marked changes in the appearance of the tonsillectomized throat. The presence of nodules of cicatricial tissue, of adhesions, and destruction of muscular tissue occur in cases that have been performed not by the tyro in the specialty but by leading rhinolaryngologists. Kenyon and Kradwell[7] have said, "It seems conservative to say that following tonsillectomy the palatoglossus and palatopharyngeus muscles are never wholly normal in their action."

Changes in the speaking and singing voice after removal of the tonsils have been forcibly emphasized by Faulkner,[8] Connor,[9] Kenyon[10] and Freudenthal.[11]

During the last five months I have added to my private case history charts a tonsil record for each patient. The following inquiries were made:

1. Have the child's tonsils been removed?
2. When were they removed?
3. By whom?
4. Why removed?
5. Has the condition improved?

I have selected for analysis 200 consecutive cases in which the tonsils were removed completely by specialists at least six months previous to the time of inquiry.

In 95 per cent. of the cases the adenoids were removed at the operation. The ages of the patients ranged from 15 months to 14 years.

The reasons given for the removal of the tonsils may be grouped as follows:

	Cases
1. Frequent attacks of colds	40
2. Obstructive symptoms (Mouth breathing, difficult nasal breathing)	46
3. Ear and mastoid infections	31
4. Attacks of acute tonsillitis	20
5. Cough	14
6. Enlarged tonsils	10
7. Diseased tonsils	9
8. Malnutrition	9
9. Cardiac and chorea	8
10. Miscellaneous (Speech defect, 2; muscular pains in extremities, 4; asthma, 2; convulsions, 1; no reason given, 4)	13

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[6] Masini: New York M. J. (Sept. 28) 1898.

[7] Kenyon and Kradwell: Ann. Otol., 1916.

[8] Faulkner: Med. Rec. **79**:40 (July) 1910.

[9] Connor: Texas State J. M. **11**:545, 1916.

[10] Kenyon: J. A. M. A. **69**:709 (Sept. 1) 1917.

[11] Freudenthal: Tr. Am. Acad. Ophthal. & Oto-Laryngol., 1918.

The symptomatology in the cases in which the complaint was of frequent attacks of colds included chiefly coryza and cough, usually with a slightly elevated temperature. Of the forty cases of this group only fourteen showed an improvement in symptoms after the removal of the tonsils and adenoids. Twenty-six, or 65 per cent., reported no improvement. Definite statements were made in eight cases that the symptoms were aggravated after the operation. I shall discuss some of the complications and sequels later.

The most important symptoms of the obstructive cases had been mouth breathing, clogged nasal passages and snoring at night. Two patients had complained of difficulty in swallowing. Of forty-six cases of this group, reports of cures or improvements after removal of the tonsils and adenoids were given in thirty-five cases, or 76 per cent. In eleven cases no improvement was noted. Of these, eight showed definite evidence of the high arched palate and imperfect coaptation of the teeth. McClanahan,[12] in 1913, called attention to the futility of operation in this type of case.

Of the thirty-one cases of ear and mastoid infections, twenty patients had had tonsils and adenoids removed in order to prevent frequent recurrences of acute otitis media. In only eight of these cases favorable reports were given, i. e., no recurrences or less frequent attacks. In one case a discharging ear developed three days after the removal of the tonsils and adenoids, in another a discharging ear followed by a mastoiditis developed one week after the operation. In the eleven remaining cases of this group the tonsils and adenoids were removed because of persistent ear discharge. In only four cases was the condition said to have been favorably influenced.

Of twenty cases, in which tonsils had been removed on account of frequent attacks of tonsillitis, three patients had developed sore throats at intervals subsequent to the operation. In each of these cases examination revealed a reddened pharynx with prominent lymph follicles.

The tonsils and adenoids had been removed in fourteen cases of persistent cough. In five of these the parents had been told that chronic bronchitis was present, in one case—asthma. Reports of cures were given in four cases. In eight cases the cough was not altered in severity by the operation; in two cases it was aggravated.

In ten cases the tonsils had been removed because of hypertrophy. There had been no symptoms. Subsequent to the operation three patients had developed frequent colds and sore throats.

Reports of diseased tonsils were given in nine cases. There had been no symptoms whatever in four of these. The rhinolaryngologist had labeled them "diseased." Following the operation, five patients had recurrent sore throats.

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[12] McClanahan: Tr. Am. Ped. Soc., 1913, p. 174.

Of nine cases of malnutrition, only three had been benefited by the removal of the tonsils and adenoids. In six there had been no more gain in weight than was noted before the operation.

There has been great difference of opinion and of statistics regarding the relation of tonsillitis to articular rheumatism and cardiac disease, from 80 (Faliber) to 1.4 per cent. (Pibram).[13] Recently St. Lawrence [14] presented very favorable results from tonsillectomy in rheumatic and cardiac cases. His patients were under the guidance of a cardiac clinic and received careful medical and social service attention. We cannot but feel that these factors play a considerable part in producing the improvement noted.

Tonsillitis is of very frequent occurrence in infancy and childhood. If the tonsils played an important rôle in the production of rheumatic and cardiac manifestations, should we not expect a greater evidence of these conditions? Is the tonsillitis frequently associated with these conditions not a manifestation of the rheumatic infection?

Of the eight cases in this group only two reported improvement. One cardiac patient had had two attacks of heart failure before the removal of the tonsils. Subsequently, over a period of two years, no attacks of decompensation had occurred. Of the five cases of chorea, three associated with cardiac lesion, four patients had had attacks after the removal of the tonsils and adenoids. Recently, I have seen two cases in which the tonsils had been removed three and five years ago, respectively. Both ran the typical course of an acute rheumatic fever with high temperature and painful, swollen joints. One developed a cardiac lesion.

Of the thirteen cases in which tonsils and adenoids had been removed—for speech defect (2 cases), muscular pains in extremities (4 cases), asthma (2 cases), convulsions (1 case), no improvement had been noted subsequent to the operation.

The statistics I have presented are not submitted as conclusive evidence. The reliability of the statements of parents is not absolute. But the facts are suggestive. Combined with the clinical impressions that I have received for a number of years in hospital and private work they have convinced me that the tonsils have too frequently been sacrificed and the risks of an operation entailed without sufficient reason.

Numerous complications following the removal of the tonsils have been described. In 1912, Koplik [15] called attention to three forms of infection following the surgical removal of the tonsils: (1) A moderate febrile reaction; (2) an acute or subacute endocarditis; (3) a severe sepsis with profuse hemorrhages and bronchopneumonia.

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[13] Quoted from Kyle: Am. J. Dis. Child. **15**:142 (March) 1915.

[14] St. Lawrence: J. A. M. A. **75**:1035 (Oct. 16) 1920.

[15] Koplik: Am. J. M. Sc. **154**:70 (July) 1912.

Dabney [16] described a case of acute rheumatic fever which developed in a child three days after tonsillectomy.

Sewell [17] reported fifty cases of serious hemorrhage with nineteen deaths following the removal of the tonsils.

Cases of general sepsis, pneumonia, lung abscess, subcutaneous emphysema, lung infarct and meningitis following tonsillectomy have been described.

In my group of cases I have seen the development of a definite lung abscess, an acute otitis media followed by a mastoiditis, and three severe cases of pharyngitis after tonsillectomy. During the past three years there were admitted to the pediatric service of Mt. Sinai Hospital seven cases of lung abscess, seven cases of bronchopneumonia and one case of lobar pneumonia which developed after the removal of the tonsils.

In selecting our cases for the removal of tonsils and adenoids we should be guided by safe and conservative principles.

1. If there are obstructive symptoms, mouth breathing (snoring at night) with no evidence of a high arched palate as the cause of obstruction, the adenoids should be removed.

2. If there is a persistent nasal discharge that does not yield to the usual therapeutic measures and in the absence of a sinusitis the adenoidectomy should be performed.

3. If the tonsils are sufficiently large to cause obstruction, difficulty in breathing or swallowing, tonsillectomy is indicated. One must not be mislead, however, by the presence of a large tonsil that appears to be obstructive, a tonsil that is rather pushed out toward the median line by the presence of a deep cervical adenitis. I have described these cases as parapharyngeal adenitis. It occurs most commonly after grippe, scarlet fever and measles.[18]

4. If the frequent occurrence of tonsillitis has produced definite disease in the tonsils, as evidenced by irregularity, raggedness and friability, tonsillectomy is indicated.

5. If there is recurrent accumulation of cheesy material in the crypts of the tonsils, or if on pressure this may be extruded from the tonsils, with the presence of a foul odor of the patient's breath and symptoms of toxic absorption, the tonsils should be removed.

6. In cases of persistent cervical adenitis following tonsillitis, whether by pyogenic or tuberculous origin, tonsillectomy is indicated.

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[16] Dabney: Ann. Otol., Rhinol. & Laryngol., December, 1913.

[17] Sewell: Med. Chron., July, 1911.

[18] Heiman: Am. J. Dis. Child. **10**:104 (Aug.) 1915.

These are the rules I endeavor to follow. But each case must be studied individually, the advantages and risks considered before recommending operation.

In conclusion, may I enlist your cooperation to banish the passionate desire, which is fast gaining ground in the profession, to remove every tonsil, and to substitute more conservative and rational principles.

APPLIED DIETETICS IN OUTPATIENT DEPARTMENTS

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If we recall the conditions prevailing twenty-five years ago in the conduct of outpatient departments in the larger hospitals, we realize much progress has been made. This is most apparent in hospitals connected with medical schools, and is largely the result of the increased use of the outpatient clinics for purposes of medical instruction. When I was a third year medical student I recall distinctly three ward visits in the Children's Hospital as the total of bedside instruction for the year in the course in pediatrics. My memory fails when I try to estimate the extent to which outpatient material was utilized for clinical lectures, but it was very meager. When as a graduate I first took charge of the outpatient department of the Infants' Hospital, clinics were practically as large as they are today. I had one nurse as an assistant, and felt myself fortunate if I could inveigle a fourth year student to help with the histories of new patients. The real burden of the clinic fell on the physician in charge. To work four hours each morning, and to see fifteen patients an hour was the standard of efficiency. Contrast this with a well organized clinic of today, with its corps of graduate physicians and interns, its clinical clerks and social workers, its clinical and roentgen-ray laboratories, the special subclinic for cases of heart disease, tuberculosis, infant feeding, posture, nutrition classes, etc. In comparison, the modern clinic seems to have reached its height of organization; certainly the quality of work is beyond anything conceived as practicable in the earlier period I have pictured. It is reasonable to suppose that the next twenty-five years will bring about other changes and innovations to add to the efficiency of medical care of ambulatory patients.

It is my wish to speak of a comparatively new department, the importance of which is becoming more and more evident as we link the social and economic conditions of the patient with his health problem. I refer to the establishment of food clinics as a very necessary and useful adjunct to the medical outpatient department. So far as I can learn there are very few institutions which have established and operated food clinics of the kind that I have in mind.

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* Received for publication, May 25, 1922.

* Read before the American Pediatric Society, Washington, D. C., May 1, 1922.

The Boston Dispensary Food Clinic was started in April, 1918, by Michael M. Davis, then director, and Miss Frances Stern of the Federal Commission of the U. S. Department of Agriculture. Lack of how to select, purchase and prepare food so as to make it appetizing, nutritious, and within the family budget, is common to all classes, but particularly so to those who attend the outpatient clinics of hospitals. The high prices caused by the war accentuated this problem, and were the direct stimulus toward the organization of the clinic. Two rooms in the dispensary were equipped with cooking utensils, stove, furniture and accessories necessary for food demonstration, and the conduct of classes. Beginning with one a week, the clinics in six months were increased to daily morning sessions. When Miss Stern went overseas, the clinic was taken over by Miss Bertha M. Wood, and has since continued under her efficient direction.

The result of three years' experience has recently been reviewed by Miss Stern, in consultation with the food committee of the dispensary. It is with the hope that our conclusions may be of help to institutions planning to establish similar clinics that I venture to bring to your attention the conclusions at which we have arrived.

The purpose of the food clinic may be called a demonstration in applied dietetics. It is intended to assist the physicians of medical clinics in carrying out food treatment. It is distinctly a part of the medical institute, in which the medical, dietetic, social, and economic problems of each case are correlated. It is not a center for the distribution of food, in which respect it differs from the diet or food stations established in many places during the war. It necessarily includes "nutrition classes," but has a much larger scope. The fundamental principle of organization is that every patient accepted must be under direct medical supervision by one who, by virtue of his specialty or experience, may be judged competent to determine the nutritional requirements of the case. A patient, for instance, might be referred by the throat department in the food clinic for a condition of malnutrition, but it would be the duty of the food clinic to see that the patient was given a general medical examination (by the pediatrician or internist) and receive from him directions for dietetic treatment. It then becomes the duty of the food clinic not only to follow the lines of treatment indicated by the physician, but to investigate through social service the home conditions, economic resources of the family, and when necessary, to bring the case into relation with proper agencies of help.

The organization of the food clinic and its relation to other departments should be prescribed very distinctly. There are many possibilities of friction and misundertandings, which we have experienced. Conflicts between social service and food workers may occur. The special department may not take kindly to the fact that its patient has been referred by the food clinic to a general medical or pediatric department. There are possibilities that the internist or pediatrist may feel at times that the dietitian has "taken the case out of his hands" or overstepped her authority. These are pitfalls into which any food clinic will fall if it is allowed to organize as a separate department without direct medical supervision. This medical supervision should be directly exercised within the food clinic, in order that all departments may work in harmony. It is not reasonable to expect that the dietitian or technical food worker is sufficiently familiar with the medical side of her cases to act at all times wisely without the advice of a physician, and she is more likely to seek that advice if she is responsible to a physician of the food clinic alone, than if she attempts to keep personally in touch with all physicians who refer patients to her.

The relation of the social service to the food clinic also is a matter of great importance. There must be a social clinic executive in the food clinic and under the direction of the chief dietitian. The first investigation of the social and economic conditions of the patient would be made by this worker, and her findings reported to the chief dietitian. By consultation it may then be determined in each case whether the continued social work should be conducted by the food clinic, or transferred as a special problem to the general social service department. Subsequent visits to the house are more likely to be made by the food worker or assistant dietitian.

In general, the organization of the food clinic is the same as that of any medical clinic and should be on the same plane.

Its special internal organization may be outlined as follows: (1) Administrative; (2) dietetic; (3) educational.

1. *Administrative.*—The head of the food clinic should, for reasons already given, be the medical consultant. To him the chief dietitian must be responsible. His duties are primarily medical, referring to the internist or pediatrist cases, which, in his judgment, require extended medical investigation, or taking the responsibility of passing the case directly to the dietitian, on the basis of his own examination. He keeps in touch with the general progress of the cases and sees that the patients report back periodically to the special clinics from which they have been referred. He is responsible for the exclusion of contagion from demonstration classes, and gives medical instruction in applied dietetics to classes, to graduates, and undergraduates.

The other members of the staff are the chief dietitian and her assistants, the trained nutrition worker, the social worker, and the clinic executives. These constitute the real working force of the food clinic, but they carry out the food treatment prescribed by the referring physician, or in case no specific directions have been made, the food treatment as prescribed by the medical consultant of the clinic. It is clear that a competent dietitian will be allowed to act on her own initiative in many cases, such as obesity, constipation, under-nourishment, but there are other groups such as renal, cardiac, diabetic, and tuberculous, which require close and frequent medical supervision—cases which the dietitian is not capable of handling alone. These must be seen frequently by the physician, who must either take the medical responsibility upon his own shoulders, or see that it is properly placed on the referring department. I cannot too strongly emphasize the importance of such medical supervision being directly exerted within the food clinic. It is quite possible that if the size of the clinic warranted, there might be several medical consultants in charge of special classes, as for instance—diabetic classes and children's nutrition classes, adult nephritic and cardiac classes, problems which would probably appeal to different types of medical food specialists. These patients, it should be distinctly understood, are not "taken out" of the medical or pediatric departments. The medical supervision exercised within the food clinic is designed only to guard against errors which might occur from lack of medical knowledge on the part of the dietitians, and to correlate the work of the medical and food clinics. The patients must, therefore, report back to the referring clinics periodically and may attend the food clinic only so long as they are medically supervised.

A food clinic should have a special record card which shall show the salient points in the medical history and physical examination, the particular object which the food clinic should strive to attain, and the date on which the patient shall report back to the medical clinic for reexamination, consultation, and advice. The liaison between the referring department and dietitian should be the medical supervisor of the food clinic, rather than the dietitian herself.

2. *Dietetic.*—The dietitian has her own definitely defined functions which she exercises directly or through her assistant workers. Briefly, these may be enumerated as follows:

I. To determine the family budget, and its possibility of supplying the necessary food which the diet calls for. It is a waste of time to order diets if there are no funds to purchase them, or no knowledge of how to prepare them. The dietitian may in her experience be able to advise a cooperative mother how to readjust her expenditures, so that the proper food may be provided, and she can instruct her in the art of utilizing cheaper products to attain the same end served by the more expensive foods.

II. When the budget is hopelessly inadequate, it is the duty of the dietitian to secure through existing associations such help as may be needed in the way of food or money, and to see that this aid is properly applied. Diet kitchens and various associations for meeting distress through contributions of food have found it profitable to appropriate a portion of their funds to the food clinic, to be used for emergency and food treatment, as they are thus saved the overhead and complications incidental to social and medical investigation and continued supervision. It is obvious that it is advantageous to carry a case through one institution, supplying all the requirements, medical, social, dietetic, then to link it up with several separately organized and operated agencies, no one of which does a complete job.

III. Selection and preparation of the food is no less important than the question of finance. We cannot assume the responsibility of dietetic treatment unless we provide instruction as to the simple facts relating to food, the methods of preparing it, etc. This has to be done in two ways: (a) by demonstrations in the class to groups of mothers and children; (b) by home visits in special cases by the food worker to help the mother apply the principles taught in the class.

IV. In our larger cities we have a very cosmopolitan population to deal with, much of it recently arrived. The average clinician knows little or nothing of the food values of Jewish, Italian, Syrian, Armenian, and similar diets. It is the duty of the dietitian to be able to think in the terms of the race she is dealing with. We cannot force an American diet at once upon all these people, but we can see that our dietitian, utilizing the foods of the nationality in the case, applies the principle of the medical foods treatment in foods familiar to them. The trouble is often due to improper balance of food which is in itself good, and we are more likely to gain the cooperation of these recent arrivals if we correct what is bad in their habits and customs, instead of trying to force an entirely new dietetic regimen upon them.

V. Still another function of the food clinician is the conduct of classes which have a special objective. We have, for instance, established classes in (1) obesity, (2) constipation, (3) malnutrition, (4) diabetes. The chief value of the group method of instruction is, of course, to economize time and effort so that the largest possible number may be reached at the minimum cost. If, however, there is no periodical medical supervision of the results of such group instruction, the best results cannot be obtained. The medical supervisor of the food clinic must be keenly interested in the work of the clinic, must feel that however much he depends upon the dietitian, the responsibility of getting results is his. This means close observation of each case, and the early separation from classes of those who are not progressing favorably, so that they may be subjected to special investigation. Practically, the routine of class and group work is carried on by the dietitian and her assistants. The medical supervisor takes as his special problem the cases that are lagging or making no response, and in his larger medical experience endeavors to supplement the efforts of the dietitian.

The nutrition class for undernourished children is one of the more important special groups of the food clinic. Such classes are being extensively organized throughout the country. The movement will undoubtedly accomplish a great deal in awakening interest in matters pertaining to nutrition, and in improving the health and physical development of the children of the country. The problem of handling the undernourished child is not, however, as simple as the layman might infer when he sees untrained persons qualify as chief nutrition workers after a two weeks' course of instruction. Malnutrition, if severe, is always primarily a medical problem, and requires close and continued supervision. The food clinic established in connection with a well organized outpatient department is the logical place for the establishment and operation of nutrition classes, which may serve not alone to meet the needs of patients drawn from the clinics, but as a school for the proper training of nutrition workers. There they can learn by actual observation the extent to which these problems of nutrition are linked with medical, social, and economic conditions, and obtain a better perspective than they are likely to under present conditions.

3. *Educational.*—The food clinic organized along the lines I have indicated would offer training to students in medicine, public health, child welfare, nursing, dietetics, and social service. The clinic executive should be a person qualified to instruct in the principles governing the organization and administration of the clinic, and the part played by social service in furnishing information to the dietitian and to the medical supervisor. The food clinician is thus free to give all her time to food instruction, helping the patient to carry out the physician's food prescriptions by virtue of her more intimate knowledge of the technical problems connected with food and its preparation for the accomplishment of specific purposes. Medical students are for the most part uninstructed in these details, and might profit greatly by didactic lectures and demonstrations given by the dietitian.

The medical consultant may also utilize the facilities of the clinic to instruct those interested in public health problems in the medical aspect of cases requiring food treatment, and in the part which continued and systematic medical supervision of the cases plays in attaining the ends sought for. Students in public health would therefore receive instruction by: (1) visits to medical clinics to observe the relationship of food clinics to other clinics; (2) work in the social service department; (3) case instruction based on actual cases, illustrating the prescribed diets in different diseases and conditions; (4) laboratory technique, as a necessary factor determining food treatment in certain diseases, such as diabetes; (5) methods of recording data; (6) educational methods employed in group teaching, as in the case of nutrition classes; (7) the literature of dietetics—including sources of information and recent works bearing on the subject of applied dietetics.

The food clinician must keep in touch with health work and publications. It should be her duty to select and prepare posters, charts, and exhibits, both for the instruction of the student and as a means of getting food ideas into the minds of her patients.

The subject of health has become a national asset. It is exploited by the newspaper, magazine, and civic organizations. Hygiene and dietetics are becoming the life work of innumerable people, some with an excellent foundation for learning, but many with a mere smattering of knowledge. The medical schools of the country are awakening to the need of authoritative teaching on these subjects of such importance to the welfare of the nation—but to be truly effective, such departments or schools of public health must have their clinics, and these must be established in connection with hospitals and dispensaries, where the principles of applied hygiene and dietetics may be studied in their practical applications.

The food clinic—whether one adopts the name or not is unimportant—should, it seems to me, become an established department of every well-organized clinic for the treatment of ambulatory patients. The plan which I have outlined has in part been effected in the Boston dispensary, and represents the general line along which we are attempting to perfect our organization. Its development will depend upon the extent to which public opinion supports the idea. We pediatricians, who are so largely concerned in the problem of nutrition, and food as a means of attaining it, can by our support of the idea of a food clinic do much to put applied dietetics upon a scientific basis, and greatly influence the public opinion as to its importance. At the same time, by the precept and example of well regulated food clinics, we may do much to clarify the subject of food in relation to diseases in our own minds, in the minds of students and hygienists, and ultimately in the thoughts and lives of the general public.

ACUTE INFECTIONS OF THE URINARY TRACT IN INFANTS AND CHILDREN SUBSIDING WITHOUT THE APPEARANCE OF PUS IN THE URINE *

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Since Escherich, in 1898, demonstrated infections of the urinary tract with the colon bacillus in infants and children to be extremely common, the subject has been discussed from almost every point of view. The route by which the infection gains entrance to the urinary tract is yet to be decided, as recently pointed out by Helmholz.[1]

In looking over the literature for the past twenty years, it is interesting to note that practically nothing new has been added during the past ten years. In 1910, I published an analysis of twenty-five cases,[2] the first dating 1901, which included virtually every clinical phase of the disease.

The one characteristic symptom is the sudden onset with high fever, frequently as high as 105 or 106 F. There is often no other symptom and the child does not seem to be "sick" enough to correspond to the degree of fever present, so that we are often in doubt as to the accuracy of the thermometer. The child may and frequently does continue to play with its toys, especially if there is no marked irritation of the bladder or urethra. In other cases, the symptoms are extremely severe, especially in the spasmophilic child.

It is generally conceded that the diagnosis must be finally decided by critical microscopic examination of the urine. The generally recognized requirements for the examination of the urine are as follows: (1) a catherized specimen in a female; (2) a thorough cleansed meatus in the male; (3) the urine to be examined immediately.

If in an uncentrifuged specimen with a hanging drop, low power, colon bacilli in numbers, and pus cells to exceed ten to the field, are present, a diagnosis of cystitis or pyelocystitis is conceded.

My thesis is: that the appearance of pus cells above a point considered normal is not necessary to establish a diagnosis of an acute infection of the urinary tract.

In 1910,[2] I pointed out that I had frequently found colon bacilli in great numbers in fresh acid urine, accompanied with characteristic symptoms, without the appearance of pus, and again in 1914,[3] I pointed

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* From the Department of Pediatrics, University of Minnesota.

[1] Helmholz: Am. J. Dis. Child. **22**:606 (Dec.) 1921.

[2] Ramsey: Northwestern Lancet **30**:523 (Dec.) 1910; Pediatrics **23**:15 (Jan.) 1911.

[3] Ramsey: St. Paul M. J. **16**:343 (June) 1914.

out that: "in many acute infections of the urinary tract, no pus is ever found, the urine containing only bacilli and some epithelial cells. A chemical examination may show a slight trace of albumin or none with the ordinary albumin test. It will, however, usually give a trace of nucelo-albumin, with the cold acetic acid test."

I have repeatedly noticed that after the acute onset of a colon bacillus infection of the urinary tract, with the characteristic high fever, that the urine although acid and containing myriads of colon bacilli remains free from pus for several days, after which pus cells begin to appear in increasing numbers. In other cases, the characteristic symptoms and fever subside after a brief period and the colon bacilli gradually disappear without the appearance of pus in the urine.

It is a well recognized fact that these acute infections with the colon bacillus frequently accompany or follow directly on the heels of some other infection, and that recurrences from time to time are not infrequent.

Colon bacilli in great numbers are found constantly in the urine over long periods of time in chronic bacterurea, and often without pus being present. In these cases the urine is practically always alkaline.

That colon bacilli are frequently present in small numbers in the urine of healthy children has recently been pointed out by Findley and Browning,[4] and confirmed by Helmholz.[5]

It is a recognized fact that mucus membranes generally are subject to infections of every grade of severity. It is rational to assume that the mucus membrane of the urinary tract is no exception to the rule.

It is also a recognized fact that very slight infections of the urinary tract are followed by severe general reactions.

My contention is that many heretofore obscure fevers in infants and children are produced by infections with the colon bacillus, these infections may be local or perhaps systemic, and that they may be diagnosed by the characteristic general symptoms and by the elimination of an increased number of colon bacilli in the urine.

REPORTS OF CASES

Case 1.—Thomas C., aged 3 years (patient of J. T. H.), was taken suddenly ill, Nov. 7, 1921, with chill and high fever. When seen by his physician a few hours after, temperature was 104.5 F., skin pale, pulse weak and rapid. General examination did not elicit anything to account for the fever. During the following three or four days, the temperature was at times as high as 104.5 F., and other times reached almost normal. Most of the time even when the temperature was high, the child did not feel especially ill and played with its toys. The physical examination remained negative.

Examination of urine, November 7, 8 and 10, showed clear acid urine, no albumin nor pus cells, but greater numbers of colon bacilli. The culture of the urine November 10 gave pure culture colon bacilli. The child was put on large doses of hexamethylenamin and large amounts of water, and the temperature became normal in a few days. All bacteria disappeared from the urine within two weeks. An examination, April 20, 1921, showed a normal urine without colon bacilli or anything abnormal.

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[4] Findley and Browning: Glasgow M. J. **97**:28 (Jan.) 1922.

[5] Helmholz: Am. J. Dis. Child. **23**:309 (April) 1922.

Case 2.—Richard M., male, aged 3 years.

During the week of February 14 to 20, this boy had a spot of pneumonia in the right upper lobe. Temperature and symptoms were characteristic of a lobar pneumococcus pneumonia. He was quite sick until the crisis on the seventh day, after which the temperature remained normal for two days. On the night of February 22, he had a sudden chill and when I saw him the following morning the temperature was 105 F. At that time he did not seem especially ill and one would not have guessed the temperature to be nearly as high. The temperature persisted more or less constant for the following forty-eight hours, and gradually reached normal.

Physical examination revealed nothing new to account for the temperature.

The urine passed in a sterile bottle and examined at once gave acid reaction, no pus, no albumin, many motile bacteria, which proved to be colon bacilli. After three or four days, the bacteria disappeared and there have been no recurrences of the fever or other symptoms; the urine remained clear.

Case 3.—Roy J., male, aged 17 months, has been rather pale for some weeks, but otherwise apparently well, taking food well. April 21, he had a sudden attack of fever; two hours after the onset the temperature was 106 F. plus per rectum. The day previous he had had a little digestive disturbance and the stools were slightly green, with considerable mucus.

A very careful physical examination showed no cause for the fever. The digestive tract was thoroughly cleared out, but the temperature persisted, varying from 103 to 106 F. for twelve hours, after which it gradually reached normal within forty-eight hours.

The specimen of urine passed directly into a sterile bottle was clear, acid reaction, no pus cells, but myriads of motile bacilli. April 23: many colon bacilli, no pus. April 24: colon bacilli, no pus. April 25: colon bacilli, considerable number of red cells, and epithelial cells, probably from the urethra. April 27: no pus cells or red cells, but many bacteria, temperature normal, and feeling very well. May 10: urine clear, acid, no albumin, no pus, no bacilli. Child remains well.

A CRITICAL STUDY OF SIXTY-ONE CASES OF ASTHMA AND ECZEMA IN INFANCY AND CHILDHOOD CONTROLLED BY CUTANEOUS PROTEIN SENSITIZATION TESTS *

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Although the subject of protein hypersensitiveness is a comparatively recent one, a great deal of literature has been published on its various aspects in the past few years. Many writers, among them Baker [1] and Peshkin and Rost,[2] have studied the frequency of the sensitization of the skin in normal persons. Schloss and Walker have also added to our much clearer understanding of the peculiar condition found only in certain persons. O'Keefe,[3] White,[4] Blackfan [5] and Baker [1] also, have made special studies on children with allergic symptoms. Nevertheless, despite all this literature, the use of the cutaneous test as an aid in diagnosis and treatment by pediatrists is still very limited, largely because of a skepticism as to the value of the results secured by this means.

The present study of sixty-one infants and children with eczema and asthma was made to show, if possible, to what extent the use of these tests is advantageous, what better results may be secured by its help, and what its limitations are. That a very large percentage of the children with these syndromes are sensitive to proteins from various sources is not new information. It is an interesting fact, however, that they most commonly derive their symptoms from more than one factor, which necessitates a thorough study of each case. The possibility of a multiple etiology must always be taken into consideration. Focal infection in this type of child plays a very important rôle. The habits of the patient, the diet, and, not of least importance, the home surroundings must be investigated carefully. In this connection, it is interesting to note that a sensitization to rabbit hair is very frequently found. Rabbit hair is commonly employed in the manufacture of articles of clothing such as furs, hats, and slippers, and also in furniture upholstering and bedding.

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* From the Department of Pediatrics, Cornell University Medical School, and the Outpatient Department of the New York Nursery and Child's Hospital.

1. Baker: Am. J. Dis. Child. **19**:114 (Feb.) 1920.
2. Peshkin and Rost: Am. J. Dis. Child. **23**:51 (Jan.) 1922.
3. O'Keefe: Boston M. & S. J. **183**:569 (Nov. 11) 1920.
4. White: Boston M. & S. J. **178**:5, 1918.
5. Blackfan: Am. J. M. Sc. **160**:341 (Sept.) 1920.

Description of Material Reported.—The material to be reported on herein consists of thirty-one cases of bronchial asthma in children ranging in age from 1 to 14 years, and thirty cases of eczema in infants and children from 5 weeks to 7 years of age (Table 1).

There were twenty-four boys out of thirty-one asthma cases, and seventeen boys out of the thirty eczema cases, thus making almost exactly twice as many boys as girls in our entire group of sixty-one cases.

The nationality of these children was not limited to any one class, and there are included negro and Jewish as well as Irish, Italian, German, Russian and French children.

TABLE 1.—Showing the Ages When the Children Were First Seen, Their Ages at the Onset of Symptoms, and the Duration of Symptoms When First Seen

	When First Seen		When Symptoms Appeared		Duration of Symptoms When First Seen	
Age Periods	Number with Asthma	Number with Eczema	Number with Asthma	Number with Eczema	Number with Asthma	Number with Eczema
Under 1 month	..	..	..	11	..	7
From 1 to 3 months	..	4	..	4	..	6
3 to 6 months	..	4	..	6	1	5
6 to 12 months	..	10	2	3	3	9
1 to 2 years	1	5	3	1	6	2
2 to 3 years	2	2	3	2	3	0
3 to 4 years	2	1	4	0	5	0
4 to 5 years	1	1	7	0	4	1
5 to 6 years	0	0	4	1	4	
6 to 7 years	3	2	0	1	2	
7 to 8 years	3	1	1	1	1	
8 to 9 years	5	None older	2	..	0	
9 to 10 years	3	..	1	..	1	
10 to 11 years	3	..	4	..	0	
11 to 12 years	1	..	..	..	1	
12 to 13 years	4					
13 to 14 years	2					
14 to 15 years	1					
Total	31 cases	30 cases	31	30	31	30

The method of procedure with each case was the same. A complete history and a thorough physical examination were recorded on charts, which forms, along with a sensitization sheet, were attached to the regular clinic records of each child. These served as a very good summary of the findings in each individual case. The children were followed up for as long a time as possible. The real difficulty was in keeping them under active medical supervision for a long enough time. As they improved the visits were fewer and fewer; and those that did not improve rapidly enough, under the treatments instituted, stopped the treatments altogether, as is often the way with dispensary patients. Table 2 will give an idea of the length of time the cases were under active treatment and under observation afterward.

All but five of the cases of bronchial asthma were observed for over one year, nine of them over a year and a half. Twenty of the eczema cases were observed for over one year, and thirteen over a year and a half.

All types of asthma and eczema are included in this report, from the mild to the very severe. No attempt has been made to classify them as to the severity or character of their symptomatology.

As to a family history of hypersensitiveness, eighteen of the cases of bronchial asthma were positive, eleven were negative and two not obtainable. Only fourteen of the eczema cases had dependable histories, ten being positive and four negative. This gives approximately 65 per cent. with positive family histories, which is fairly close to the figures of Schloss,[6] who found 59 per cent. of eighty children positive.

Thirteen of the children with asthma had, either at the time first seen by me or at an earlier date, an eruption which evidently was eczema. Four of these had both eczema and urticaria. Five others had had urticaria but no eczema.

TABLE 2.—Showing Lengths of Time All Cases Were Under Treatment and the Total Observation Period at the Present Time

	Number of Cases Under Treatment		Number of Cases Under Observation	
Period of Time	Asthma	Eczema	Asthma	Eczema
Under 1 month	3	6		
1 to 3 months	6	10	None for a shorter time	
3 to 6 months	9	10	1	4
6 to 12 months	7	3	4	6
12 to 18 months	6	0	17	7
18 to 24 months	None longer	0	8	6
Over 2 years	..	1	1	7
Total	31	30	31	30

Six of the asthmatic group gave a history of very apparent food idiosyncrasies as follows: 2 to eggs alone; 1 to eggs, beef, and fish; 1 to oatmeal; 1 to mustard; and 1 to oatmeal, pears, cheese and bananas. Ten of the eczema group showed idiosyncrasies to foods as follows: 7 to egg alone; 1 to fish; 1 to egg and wheat; and 1 to egg and oatmeal.

Fluoroscopic and roentgen-ray studies were made in all but four of the asthma cases, and "normal" chests were found in only six. Three cases proved to have tuberculous lesions, one being parenchymatous, which went on to healing, and the other two in the form of tuberculous peribronchial and tracheal glands. The common findings in the remaining cases were a chronic fibrous bronchitis with a diffuse peribronchial thickening and congestion, and very frequently a hilus fibrosis of considerable extent. Emphysematous changes were found in a considerable number.

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[6] Schloss: Am. J. Dis. Child. **19**:433 (June) 1920.

Of the eczema cases, fourteen were breast-fed when first seen, and four more had been breast-fed at the time of the first appearance of the eruption. In eight cases the eczema had appeared on weaning and in the four remaining children only appeared at the later period of life, when on a much more varied diet than the others.

The Cutaneous Tests.—The cutaneous test was used exclusively in this work. The conclusions of Schloss, who has probably had the widest experience on the comparative value of the cutaneous versus the intracutaneous method, are agreed with by most investigators of the subject. The method of procedure has been described repeatedly in the literature and does not require repetition here.

In interpreting the readings, positive reactions were graded into four different degrees as follows:

1 +, those with a wheal between 5 and 10 mm. in diameter.
2 +, those with a wheal between 1 and 1.5 cm. in diameter.
3 +, those with a wheal between 1.5 and 2 cm. in diameter.
4 +, those with a wheal larger than 2 cm. in diameter.

A single doubtful reaction (i.e. with a wheal greater than the control but not 5 mm. in diameter) was disregarded unless it was present on several repeated trials, when it was taken into the final consideration of the case.

Summary of the Skin Tests Performed.—The skin test was employed in the entire number (sixty-one) of cases here reported; all other cases seen but not tested were omitted.

Complete routine tests were performed in nearly all the cases of bronchial asthma, but this was neither possible nor necessary in the eczema group because of their much more limited diets at their earlier age. In all, 4,520 tests were performed, including 979 repeated tests.

Asthma Cases: A total of 3,722 tests were done on the thirty-one children, 842 of these being repeated tests. This makes an average of ninety-six different proteins tried in each case, plus twenty-eight repeated. The greatest number tried in any case was 139 different proteins with ninety-nine repeated tests, and the least number was twenty-four different proteins.

Eczema Cases: A total of 798 tests were performed on the thirty children in this group, 137 of the tests being "repeats." Thus an average of twenty-two different proteins were tried per patient with from four to five "repeats." The maximum number in any case (on one of the older children) was 110 different proteins with thirty-nine "repeats," and the minimum was four tests on a very young breast-fed infant whose mother refused permission to do more.

In summarizing my results, the repeated tests were not counted individually, but the result with each protein, after all "repeats" were done, was recorded on the basis of the most constant and probable finding in conjunction with the clinical record of the case.

Number of Positive and Doubtful Reactions.—There were a total of 307 positive and doubtful reactions in all, making only about one in every eleven or twelve tests performed which were either positive or doubtful. There were only 128 positive reactions, making only one in every twenty-eight or twenty-nine tests, an average of two per patient.

Number of Sensitive and Nonsensitive Cases.—Of the asthmatics, eleven showed absolutely no positive reactions and three others only such slight reactions as to consider them finally nonsensitive. The remaining seventeen gave eighty-two positive reactions, and 170 positive and doubtful together. This makes an average of five positives per patient and ten positive or doubtful. There were four with only one positive, five with only two positive, and three with only three positive, the remainder all showing more than three, and in one case as many as seventeen positive reactions.

TABLE 3.—SHOWING THE PER CENT. OF NONSENSITIVE PERSONS IN VARIOUS HYPERSENSITIVE GROUPS *

	Type of Cases Studied	No. of Cases	Percentage Nonsensitive
O'Keefe	Eczema in infants	70	24.5
Schloss	Eczema in infants under 16 months	53	24.5
	Eczema in children over 16 months	24	58
White	Eczema in children	56	20
Blackfan	Eczema in children	27	18.5
Strickler	Eczema in children	46	26
Walker	Bronchial asthma in adults and children	400	52
Sanford	Asthma and hay fever in adults and children	800	62.5
Fox and Fischer	Eczema in adults	60	41
Ramirez	Eczema in adults	78	48
Author	Eczema in infants and children	30	43
	Bronchial asthma in children	31	45

* A comparison of the above figures with those of Baker, or of Peshkin and Rost for normal children, is very striking in that positive or even doubtful reactions are extremely uncommon in the latter.

Of the eczema cases, thirteen gave absolutely no positive reactions and four others gave only doubtful reactions, which, however, had to be considered as sensitizations because of the clinical findings in these children. The 114 positive and doubtful reactions were therefore divided among seventeen children, giving an average of seven per case. There were forty-six positives alone, in thirteen children, or three and a half positives per patient.

The percentage of sensitive to nonsensitive cases found in children with allergic symptoms varies in different groups studied by different writers. These figures are given in Table 3.

The Reactions Given by the Different Proteins.—The results of the reactions which the various proteins gave are best shown by the summary in Tables 4 and 5.

TABLE 4.—SUMMARY OF THE RESULTS OF THE SKIN TESTS—ECZEMA CASES

Proteins	Cases	Neg.	4+	3+	2+	1+	±	Proteins	Cases	Neg.	4+	3+	2+	1+	±
Asparagus	5	4	..	..	..	..	1	Pear	5	4	..	..	..	..	1
Banana	9	8	..	1	..	..	..	Pineapple	2	1	..	..	..	1	..
Barley	24	18	..	..	..	1	5	Plum	3	2	..	..	..	..	1
Bean	7	6	..	..	1	..	..	Potato	25	21	..	..	1	..	3
Beef	8	7	..	..	..	..	1	Raspberry	2	1	..	..	..	..	1
Blackberry	3	2	..	..	..	..	1	Rice	22	21	..	..	..	1	..
Buckwheat	7	6	..	..	..	..	1	Rye	17	15	..	..	..	1	1
Casein	6	5	..	..	..	..	1	Shad	2	1	..	..	..	1	..
Celery	6	4	..	..	..	..	2	Spinach	13	12	..	..	..	..	1
Cheese	4	3	..	..	..	..	1	Turnip	6	5	..	..	..	..	1
Chicken	15	11	..	..	..	1	3	Turkey	3	1	..	..	..	..	2
Coffee	8	7	..	..	..	..	1	Wheat, whole	29	23	..	..	..	4	2
Corn	7	5	..	..	1	..	1	Wheat, leucosin	5	3	..	..	..	1	1
Ovomucoid	6	2	1	1	1	..	1	Bacteria							
Egg, whole	28	16	..	1	4	4	3								
Egg, white	13	5	..	..	3	2	3	Staphylococcus pyogenes aureus	2	1	..	..	..	..	1
Egg, yolk	15	10	..	..	1	2	2								
Herring	3	2	..	..	..	..	1	Staphylococcus pyogenes albus	2	1	..	..	..	..	1
Lactalbumin	7	5	..	..	2	..	..								
Lamb	12	11	..	..	..	1	..	Staphylococcus pyogenes citreus	2	1	..	..	..	..	1
Lima bean	6	5	..	..	1	..	..	Remainder all neg.							
Cow's milk	29	25	..	..	1	3	..	Animal Emanations							
Mustard	2	1	..	..	1	..	..	Goose feathers	4	3	..	..	..	..	1
Oat	26	23	..	..	..	1	2	Horse dander	5	4	..	..	..	..	1
Peach*	4	3	..	..	1*	..	1	Horse serum	4	3	..	..	..	..	1
Peanut	3	2	..	..	..	1	..		—	—	—	—	—	—	—
Total											1	3	17	25	51

* In one case the stock peach protein was found doubtful (±), but when a sample of some fresh, home-cooked peaches was tried, the reaction was 2+.

TABLE 5.—SUMMARY OF THE RESULTS OF THE SKIN TESTS—ASTHMA CASES

Proteins	Cases	Neg.	4+	3+	2+	1+	±	Proteins	Cases	Neg.	4+	3+	2+	1+	±
Almond	25	24	..	..	..	..	1	Oyster*	22	21	..	..	..	1	..
Banana	30	27	..	..	1	..	2	Parsnip	23	22	..	..	..	..	1
Barley	30	29	..	..	..	..	1	Pea	27	26	..	..	..	1	..
Bean	25	24	..	..	..	..	1	Peach	26	25	..	..	..	..	1
Beef	28	24	..	..	3	..	1	Pear	26	23	..	..	..	1	2
Blackberry	24	23	..	..	..	..	1	Perch	22	20	..	..	..	1	1
Bluefish	24	23	..	1	..	..	..	Pike	23	22	..	1	..	..	..
Buckwheat	24	23	..	..	..	..	1	Pineapple	15	14	..	..	..	1	..
Cabbage	24	22	..	..	..	..	2	Pork	25	24	..	..	..	..	1
Carrot	26	24	..	..	..	1	1	Potato	30	27	..	..	1	1	1
Cauliflower	24	23	..	..	..	..	1	Radish	24	23	..	..	..	..	1
Celery	23	22	..	..	..	1	..	Rice	30	29	..	..	..	..	1
Cheese	24	22	..	..	..	1	1	Rye	30	29	..	..	..	..	1
Chicken	29	26	..	1	1	1	..	Salmon	22	21	..	..	1	..	..
Clam*	23	22	..	..	..	..	1	Shad	22	21	1	..	..	..	..
Cocoa	24	22	..	..	..	..	2	Sole	21	20	..	1	..	..	..
Codfish	26	25	1	..	..	..	..	Squab	23	21	..	..	..	..	2
Coffee	27	24	..	..	..	1	2	Squash	24	19	..	..	..	..	5
Corn	25	24	..	..	..	..	1	Turnip	23	22	..	..	..	..	1
Duck	26	22	..	..	1	1	2	Turkey	23	20	..	..	..	1	2
Ovomucoid	17	14	2	1	..	..	..	Veal	24	21	..	..	..	2	1
Egg, white	16	12	..	3	..	1	..	Wheat (whole)	30	29	..	..	..	..	1
Egg, whole	28	25	..	1	2	..	..	Wheat (globulin)	9	8	..	..	..	..	1
Egg, yolk	16	12	..	2	..	2	..	Bacteria							
Fig	25	20	..	..	..	..	5								
Goose	25	21	..	..	1	1	2	Staphylococcus pyogenes aureus	26	25	..	..	..	..	1
Grapefruit	25	24	..	..	..	..	1								
Guinea fowl	19	17	..	..	1	1	..	Staphylococcus pyogenes albus	26	25	..	..	..	..	1
Haddock	23	21	1	..	..	..	1	Diphtheroid bacillus	26	24	..	..	..	..	2
Herring	25	24	..	1	..	..	..	Remainder all neg.							
Lactalbumin	18	15	..	..	2	..	1	Animal Emanations							
Lamb	28	25	..	..	1	2	..	Cat hair	28	22	..	..	..	2	4
Lentil	25	24	..	..	1	..	..	Dog hair	26	20	..	..	..	2	4
Mackerel	22	21	..	..	1	..	..	Chicken feathers	29	22	..	..	1	3	3
Milk (cow's)	30	27	..	..	..	2	1	Goose feathers	29	22	..	..	..	3	4
Milk (goat's)	2	1	..	..	1	..	..	Sheep wool	27	25	..	..	..	..	2
Milk (Dryco)	2	1	..	..	..	..	1	Horse dander	29	22	..	..	1	2	4
Mustard	27	24	..	2	..	1	..	Rabbit hair	22	14	1	5	1	..	1
Oat	29	26	..	..	..	..	3	Pollens† (31 in all)	13	8	..	..	2	1	8
Onion	29	26	..	..	..	..	3		—	—	—	—	—	—	—
Total‡											6	19	21	37	88

* Interesting to note that these were negative in a case with general fish sensitization, but who had never been offered any variety of sea food.

† All negative except 2+ to corn pollen and short ragweed; 1+ to corn pollen, and ± to corn pollen (3), cherry, clover, locust, oak, and rye (1 each).

‡ Pollens not included in totals.

The Proteins Most Frequently Giving Positive and Doubtful Reactions.—An analysis of the frequency with which the various proteins give definitely positive reactions (without regard for the doubtful ones), will probably give the truest estimation of their relative places as causative factors in allergic syndromes. Table 6 has been prepared on this basis. Positive reactions were most commonly secured, in the cases of bronchial asthma with the proteins of rabbit hair, egg (both white and yolk), chicken feathers, lactalbumin, beef, lamb, mustard, horse dander, goose feathers, and chicken. In the eczema group the order is egg (both white and yolk), lactalbumin, lima bean, corn, wheat, whole cow's milk, bean, and banana. When we average the findings in all the cases, we find the most common offenders are egg (both white and yolk, with ovomucoid positive in all the cases in which egg white was positive), rabbit hair, cow's milk (more especially the lactalbumin which is very frequently positive where whole milk is only doubtful), mustard, chicken feathers (with goose feathers slightly less often),

TABLE 6.—The Proteins Most Commonly Giving Positive Reactions—in Their Order of Frequency

No.	Proteins	No. of Cases Tested	Per Cent. of Positives	No.	Proteins	No. of Cases Tested	Per Cent. of Positives
	Asthma Cases (31)						
1.	Rabbit hair	22	33	15.	Dog hair	26	8
2.	Egg-white	16	25	16.	Duck	26	8
3.	Egg yolk	16	25	17.	Goose	25	8
4.	Ovomucoid	17	18	18.	Veal	24	8
5.	Chicken feathers	29	14	19.	Cat hair	28	7
6.	Lactalbumin	18	11	20.	Cow's milk	30	7
7.	Beef	28	11	21.	Potato	30	7
8.	Egg, whole	28	11	22.	Turkey	23	4.5
9.	Lamb	28	11	23.	Celery	23	4.5
10.	Mustard	27	11	24.	Pear	26	4
11.	Horse dander	29	10	25.	Coffee	27	4
12.	Goose feathers	29	10	26.	Carrot	27	3.5
13.	Chicken	29	10	27.	Banana	30	3
14.	Guinea fowl	19	10				
	Eczema Cases (30)						
1.	Ovomucoid	6	50	10.	Bean	7	14
2.	Egg-white	13	38	11.	Banana	9	11
3.	Egg, whole	28	32	12.	Lamb	12	8
4.	Lactalbumin	7	28	13.	Chicken	15	7
5.	Egg yolk	15	20	14.	Rye	17	6
6.	Lima bean	6	16	15.	Rice	22	4.5
7.	Corn	7	14	16.	Barley	24	4
8.	Whole wheat	29	14	17.	Potato	25	4
9.	Cow's milk	29	14	18.	Oat	26	4
	Both Asthma and Eczema Cases (61)						
1.	Egg-white	29	31	13.	Goose feathers	33	9
2.	Rabbit hair	24	29	14.	Horse dander	34	9
3.	Ovomucoid	23	26	15.	Beef	36	8.3
4.	Egg yolk	31	22.6	16.	Shad	24	8.3
5.	Egg, whole	56	21.5	17.	Goose	29	7
6.	Lactalbumin	25	16	18.	Duck	30	7
7.	Mustard	29	14	19.	Veal	28	7
8.	Chicken feathers	33	12	20.	Dog hair	28	7
9.	Cow's milk	59	10	21.	Whole wheat	59	6.8
10.	Lamb	40	10	22.	Cat hair	33	6
11.	Guinea fowl	21	9.5	23.	Potato	55	5.5
12.	Chicken	44	9				

lamb, chicken and poultry in general, and so on down the list with horse dander, beef, veal, dog and cat hair, whole wheat, and potato following.

It is of interest in this connection to note the findings of Baker working with children having anaphylactic symptoms. He found the order of frequency of sensitization to foods to be oats, potato, eggs, pea, rice, casein, beef juice and chicken. This is quite at variance with my figures in so far as I only found one positive reaction in fifty-five children tested out with oats, three positive in fifty-five tested with potato, one in forty for peas, one in fifty-two for rice, and no positives and only two doubtful in twenty-two tested out with casein.

When, however, the number of doubtful reactions secured are combined with the number of positives, a somewhat different order is found.

(a) In the asthmatic cases: Rabbit hair, egg, chicken feathers, goose feathers, horse dander, dog hair, cat hair, fig, lactalbumin, duck, goose, beef.

(b) In the eczema cases: Egg, lactalbumin, corn, chicken, barley, wheat, casein, lima bean, potato, whole cow's milk, bean, beef.

In comparing the findings of various authors, as to the proteins to which children are most commonly sensitized, one sees that egg ranks very high in all the reports. The sensitization to milk is also very common. Although potato was found frequently by O'Keefe and Baker and fairly often by Walker (all ages), I did not find it nearly as often as I did other proteins. The same is true of casein, to which only two children were sensitive (two infants who gave a doubtful reaction to casein with a 2 + reaction to lactalbumin).

It is very interesting to note that the animal epidermal proteins give such a high percentage of positives and are so frequently one of the main etiologic factors in the asthmas of children. Walker[7] found a similarly high percentage in studying adults and children. He reports 17 per cent. positive to horse dander, as compared to 10 per cent. in my series. His figures for feathers were much lower, being only 0.75 per cent., whereas I found 14 per cent. positive.

A very recent finding, and one of apparently great interest to those of us who see cases of hypersensitiveness, is the very large percentage of children who show a sensitization to rabbit hair. Dr. Samuel Bell of New York City last year reported[8] a case of bronchial asthma in a girl of about eight years whose skin reaction to rabbit hair was markedly positive and whose symptoms cleared up almost at once upon the removal of a "felt" tam-o-shanter hat proven to be made partly of rabbit hair. He has informed me [9] that he has observed approximately 36 per cent. of positives to rabbit hair among his cases of bronchial asthma in children. Dr. A. Bret Ratner, working separately in my class at the New York Nursery and Child's Hospital Outpatient Department, has found eight positive cases of rabbit hair sensitization, and has reported six of them [10] along with one of my own, whose case history is given below. Working at the same time, I was able to find seven of the thirty-one asthmatics here reported definitely sensitive to rabbit hair, and to relieve four of them almost completely, two of them noticeably, and one but slightly, by removing the offending objects wherever possible. I refrain from using the word "cured" in the first four cases because I feel that no case should be reported cured which has not been absolutely without symptoms for a period of at least six to twelve months, and preferably longer. A positive reaction does not mean immediate cessation of symptoms upon the removal of the offending objects made with rabbit hair,because,as in some of the cases mentioned above, a multiple sensitization is often present and the additional factors in each case must be ruled out. The good result mentioned by Ratner was only secured by first completely eliminating all other causes. It will be instructive to insert here a detailed record of this case as an example of the multiplicity of causes sometimes found.

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[7] Walker: Arch. Int. Med. **22**:466 (Oct.) 1918.

[8] Bell: Tri-City Meeting of the Pediatric Section of the New York Academy of Medicine, Dec. 5, 1921.

CASE 1.—Jan. 10, 1921, a Russian Jewish boy, aged 9½ years, was sent to me from the dispensary of another hospital for skin tests and treatment.

Family History.—His family history was entirely irrelevant, except for the fact that his mother was suffering from chronic pulmonary tuberculosis.

Personal History.—He had had measles and chickenpox and a convulsion of unknown etiology at 3 years of age. Between 5 and 6, he had several attacks of urticaria accompanied by nausea and vomiting, and during this time there appeared an eczema on the face, arms, chest and back, which condition was still present, though very mild at the time when he first applied for treatment for his asthma. At 8½ years he had a severe attack of bronchitis and from then on began to get frequent attacks of a typically asthmatic character. He had had his tonsils and adenoids removed with marked relief all summer. During the fall and winter of 1920, however, he had had several "head-colds," each of which seemed to induce a fresh attack of asthma. These attacks would come on about every three weeks, last from two to three days and go away, leaving him absolutely free in the interim except for a nasal congestion. His mother was questioned closely and assured me that he used a feather mattress, a feather pillow, and a feather quilt of which she brought me specimens. He drank much milk, ate a general diet, but was usually very constipated.

Examination.—His physical examination was irrelevant, except for a nasal obstruction, a mild eczema of the face and chest, and the usual lung findings during an attack only. A Wassermann test was negative.

A roentgen-ray examination of his lungs showed nothing save a slight hilus fibrosis.

His V. Pirquet test gave a faintly positive reaction.

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[9] Personal communication.

[10] M. Clin. N. America **5**:1129, 1922.

Jan. 19, 1921, he was first tested out by the cutaneous skin test and the following positive reactions were found: Lactalbumin, two plus; beef, two plus; goat's milk, two plus; cow's milk, one plus; lamb, one plus; veal, one plus; Dryco Dried Milk, plus minus; squash and perch were doubtful, while human milk and casein were negative, as were all the other tests done at that time.

Treatment.—After observing him for about a month on a so-called milk-free diet which was not very rigidly held to, his relief was so slight that hypodermic desensitization was decided on and begun February 28, on which day his tests were repeated. This time he gave a two plus reaction to a 1:100 dilution of cow's milk. A dilution of 1:400 of lactalbumin gave a definite one plus reaction. His first injection was 0.2 c.c. of a 1:5,000 dilution of whole cow's milk to which he gave a negative skin test. He received injections every four or five days up to May 13, a period of two and a half months, during which time he had had but one short, very slight attack. His skin condition, while at first aggravated by these injections, later cleared up entirely. April 1 lactalbumin gave only a positive (one plus) reaction and April 12 whole milk gave a doubtful reaction, the 1:100 dilution being almost negative. On this day he was tested out for the first time to rabbit hair and showed a three plus reaction. This was considered significant and the mother was asked to bring in samples of the materials with which his mattress, pillow and quilt were stuffed. This she did, but no rabbit hair was among them. She was told to eliminate from the home all articles which could possibly be made with rabbit hair.

May 13, following the injection of 0.5 c.c. of a 1:500 dilution of cow's milk, the patient developed a very severe attack of asthma lasting several days. It was decided to continue the desensitization more slowly and by mouth. This was done and the dose was increased under careful supervision. He had had no attacks during all this time save the one reaction. He went to the country July 5 and, while away, had an attack lasting two days. On his return, his desensitization had progressed so far that he was taking one glass of whole milk daily. August 16 his skin rash returned and was quite troublesome until the milk was boiled and the amount temporarily diminished, when the skin cleared up. September 27, he developed a severe attack of asthma following an ordinary cold. He was found to have a definite nasal and postnasal infection with a catarrhal otitis media. He was then taking one pint of milk daily. Because of a definite nasal obstruction and some tenderness over the right maxillary antrum, he was sent to a nose and throat specialist who reported a definite clouding of the ethmoid cells and of the right maxillary antrum, with a large polypoid degeneration of the right middle turbinate. This was obstructing proper drainage and breathing. It was considered inadvisable to wash out the sinuses in so youthful a patient, but, in the last week of October, the polypoid degeneration was removed under novocain. During the next week he had such a severe attack of asthma (from the lighting up of the sinusitis?) that he had to receive adrenalin hypodermically.

He had several slight attacks during the next month, but December 6 I saw him in such a severe attack that he had to be admitted to the hospital at once, where he was only relieved by morphin after several injections of epinephrin had failed to relieve. While in the hospital, Dr. Ratner's attention was called to this case and he visited the home in a search for rabbit hair. The boy's quilt—one that had been added recently on top of his ordinary coverings—was found to contain rabbit hair and was gotten rid of. From December 25 to the end of January (1922), the boy was in the country. He has since returned to his home. He has had only one attack since his return home and that one very mild. He is at present drinking one quart of milk daily with no bad effect. His skin is clear. His sinuses were examined early in February and were found to have cleared up almost entirely. His skin tests have become completely negative to milk.

This boy illustrates well the complexity of many of these cases. There seems to be little doubt here of the combined etiology—milk and rabbit hair sensitizations plus an additional focal infection. Of course, it is entirely too early to state whether he will remain well, but he is nevertheless markedly improved at the present time.

This case is more or less typical of the majority of the cases one meets. It is rare to find a single etiologic factor (Case 3), but very common to have many factors playing their parts in the causation of the symptoms. In the classification which follows the frequency of secondary infection and focal infection is striking.

CLASSIFICATION OF CASES INTO GROUPS, WITH THE AID OF THE CUTANEOUS TEST, AND THE RESULTS SECURED IN EACH GROUP

BRONCHIAL ASTHMA

1. Sensitive: (17)—(*A*) To food alone—4 cases. (1 to eggs, fish, and meat—improved; 1 to eggs, chicken, and poultry, etc.—markedly improved; 1 to mustard alone—cured; 1 to eggs and potato—cured.)

(*B*) To food plus a tuberculous infection—1 case. (Marked sensitization to eggs; given a short series of hypodermic injections to egg before sending to an institution for tuberculosis—now much improved.)

(*C*) To food plus a tuberculosis with a secondary infection in addition—1 case. Sensitive to meats (especially to beef); (permission to send away refused—unimproved.)

(*D*) To food plus animal epidermal proteins—2 cases. (1 to mustard, rabbit hair, lactalbumin and cheese—somewhat improved; 1 to rabbit hair, coffee, and less so to horse dander, wheat and squash—improved slightly [co-operation poor].)

(*E*) To food plus animal epidermal proteins with a secondary infection in addition—2 cases. (1—the case cited above—sensitive to rabbit hair, milk, meats, plus a nasal sinus infection—marked improvement—too recent to call cured as yet; 1 to horse dander, pineapple, carrots and oats, plus badly diseased tonsils—marked improvement.)

(*F*) To pollen proteins—1 case. To corn pollen—cured of both seasonal urticaria and all-year asthma by hypodermic treatment.

(*G*) To animal epidermal proteins with a secondary infection—6 cases, 4 of these to rabbit hair plus a focal infection which required treatment—1 cured; 2 marked improvement, and 1 improved somewhat; 1 was sensitive to chicken feathers and goose feathers, and had badly diseased tonsils and adenoids—cured; 1 reacted positively to an extract of the dust from his bedroom, and also to chicken feathers and goose feathers and dog hair, plus in addition badly diseased tonsils—marked improvement.

2. Nonsensitive: (14)—(*A*) Tuberculosis (pulmonary) was the sole cause in one case, now free of asthma. The tuberculous lesion is disappearing.

(*B*) Specific etiology undetermined in one case cured by change of residence to another part of the city. Attacks recur when he returns to his downtown home. No sensitizations.

(*C*) Purely focal infections—12 cases, 6 cured; 2 markedly improved; 3 moderately improved, and 1 unimproved because focus remains, due to the fact that permission to have badly diseased tonsils removed was refused. (Vaccine gave temporary improvement.)

ECZEMA CASES

1. Sensitive: (17)—(*A*) To food alone—11 cases; 5 cured; 3 well (passive desensitization); 2 marked improvement, and 1 somewhat improved.

(*B*) To food and pollen proteins—1 case of multiple food sensitization (egg being the main offender) plus a sensitization to short ragweed—markedly improved.

(*C*) To food with definitely wrong habits of feeding in addition—5 cases; 1 case cured; 2 marked improvement; 1 somewhat improved (very recent), and 1 unimproved when last seen.

2. Nonsensitive: (13)—Due to wrong habits of feeding (frequent, numerous feedings or over-feeding as to type of food or both) or in some of the cases to local irritations—13 cases; 5 cases cured; 5 markedly improved under treatment; 1 moderately improved, and 2 cases unimproved with etiology undetermined.

It will be noticed that among the asthma cases there are twelve patients who were cured, eight markedly improved with only a rare, mild attack, or in two no attacks but too recent to report as cured, seven somewhat improved having much less frequent and more mild attacks than before treatment, one but slightly improved, and two unimproved. There were, therefore, 39 per cent. cured and 26 per cent. very markedly improved. Only three cases, or 10 per cent., fall into the class which were not benefited.

The results in the eczema cases are not claimed to be due only to the skin tests, for children of this type tend to get well without any treatment over such a period of time as these were under observation. But I do feel that the improvement was in most cases exceptionally rapid and especially in those with a determinable sensitization to a protein which could readily be eliminated. Recurrences were also rare because of the warnings given the mothers as to the sensitization. No cases of skin sensitization to any of the bacterial proteins were found in this series of cases.

DISCUSSION

The greatest difficulty met with in studying cases of asthma and eczema is in properly evaluating the various etiologic factors in each person. It is rare to find a single cause, the elimination of which stops all symptoms at once. Such a case, however, is that of the girl (Case 3) who was very sensitive to mustard alone and who has never had an attack of asthma, urticaria, or "biliousness" since the removal of mustard from her diet more than a year and a half ago. Usually, however, there is a multiple etiology with sensitizations to several foods, or animal emanations or pollens. Occasionally, a sensitization is combined with an infectious condition such as a tuberculous process in the chest, or a focal infection with a secondary invading organism. Removing only one or two of these factors will at times give marked relief, but again one must search elsewhere and eliminate all other causes as well. Rabbit hair sensitization is a common cause of bronchial asthma in children. A hypersensitiveness to eggs, milk, mustard or feathers is also frequent.

In treating these cases by means of oral or hypodermic desensitization, the cutaneous tests are of great help as a guide in the progress of the desensitization.

Some important points in regard to the cutaneous test, which have been mentioned in the literature before, are the following:

1. *The Relative Specificity of the Reactions.*—The cutaneous test is not absolutely specific but relatively so. For example, in almost every case in which a strongly positive reaction to egg was secured, there was also a positive reaction, although usually less marked, to chicken and to the poultry group of proteins, and occasionally even to chicken feathers. Moreover, when desensitization is being attempted, it is usually to be observed that not only does the skin reaction to the protein being injected grow smaller gradually, but also the reactions to the closely related proteins.

2. *The State of Anti-Anaphylaxis or Temporary Desensitization.*—A negative reaction is not always final because of this phenomenon. A hypersensitive individual may be in this state for a variable period following exposure to a large amount of the offending protein which gave rise to the usual symptoms. One must guard against this as much as possible by not performing the tests for a reasonable interval after the last attack, and also by repeating the tests wherever possible at a later date.

3. *The Occasional Lack of Correspondence Between Skin Reactions and Clinical Findings.*—(*a*) Quite infrequently one finds a case (Case 12 after receiving treatment) in which the skin reaction is positive without any symptoms appearing upon exposure to the protein. These cases must be considered as potential sensitizations. It is probable that very large amounts of the protein would bring out some manifestations of the hypersensitiveness. This seems quite possible when we remember that there seems to be no relationship between the size of the skin reaction and the severity of the symptoms.

(*b*) Repeatedly negative skin reactions are sometimes found in a case where there is a definite clinical food idiosyncrasy. Though rare, this condition has been observed (Schloss[6]) especially in infants where it is most frequently manifested by gastro-intestinal symptoms brought on by a food, very often cow's milk, to which the skin shows no sensitization. This is believed to be due to a lack of skin sensitization alone.

4. *The Presence of a Highly Sensitive Skin.*—The skin tests are of no use where a positive control test is always present. Certain persons are known to possess extremely sensitive skin (factitious urticaria). This condition makes the interpretation in these cases very difficult if not impossible. It must be remembered, however, that a skin reaction in order to be positive, must have the typical formation of pseudopod-like processes extending out from the wheal. A wheal in which there are no such processes must be considered negative even in the presence of a definitely negative control.

SUMMARY

1. Thirty-one cases of bronchial asthma in children from 1 to 14 years of age, and thirty cases of eczema in children from 5 weeks to 7 years of age are described and studied.

2. The standards used in the interpretation of the cutaneous reactions are set down.

3. A total of 4,520 tests were performed, 979 of these being tests with the same proteins repeated. An average per patient of ninety-six different proteins (with twenty-eight repeated) were tried on the asthmatic group, and twenty-two different proteins (with five repeated) on the eczema group.

4. There is a much greater incidence of protein sensitizations in children with asthma and eczema than in normal children.

5. Approximately one in every twenty-eight or twenty-nine tests performed gave a positive reaction, and one in every eleven or twelve tests was either positive or doubtful.

6. As many as fourteen of the asthma cases and thirteen of the eczema cases gave no indication of hypersensitiveness as determined by skin tests.

7. The proteins of egg, rabbit hair, cow's milk (especially the lactalbumin portion), mustard, chicken feathers and goose feathers, lamb, chicken, goose and duck, gave the most frequent positive reactions.

8. A classification is given of the individual cases into sensitive and nonsensitive, and further into subgroups according to the type of proteins to which they were sensitive (i. e., whether food, animal epidermal, pollen, or bacterial), with the results secured in each subgroup. No cases were bacteria sensitive.

9. The importance of focal infections as an etiologic factor in these children is stressed.

10. Sensitization to the proteins of rabbit hair, which is very commonly found in all homes, is a frequent occurrence.

11. The multiplicity of causes with the consequent necessity of intense individual study is very striking.

12. Occasional findings which limit the usefulness of the protein sensitization test are mentioned.

REPORT OF ADDITIONAL CASES

ASTHMA

Case 2.—M. R., a Jewish boy, aged 3 years, had suffered from asthma since 1 year old. His mother remembered that she had had eczema in her childhood. Eggs, beef juice, or any kind of fish made the boy "deathly" sick, with nausea, vomiting, hives, and asthma. He was brought to the hospital for relief from the more or less continuous asthma and wheezing respirations. He had in addition a chronic nasal discharge, and a mild papular eczema of the face, chest, and back. Skin tests showed a marked sensitization to very many foods, among them eggs, chicken, poultry, all fish (except lobster and oyster, which he had never eaten), banana, beef, pears, etc. Limitation of diet was naturally a very difficult procedure, and was never properly carried out because of a continued loss of weight, to which the mother objected. She preferred that he suffer from the mild attacks of asthma rather than lose weight on a very rigid diet. Hypodermic desensitization to egg-white was started but not continued very long because of the further objection on the part of the mother to this method. These few treatments, however, caused the cessation of the nasal discharge. At the same time, his eczema cleared up entirely, and his asthmatic attacks were exceptionally mild during this period. He is at present in better condition than ever before because the mother is able to control his diet fairly intelligently with her knowledge of his sensitizations.

Case 3.—J. W., a girl, aged 12 years, suffered with attacks of asthma since 10 years old. She would have an attack about every third month. It was usually quite severe, coming on with vomiting and accompanied by crops of hives. She knew that delicatessen foods always seemed to make her sick. Her skin tests showed a strongly positive reaction to mustard and a doubtful one to oats. Put on a diet free of these two articles, she had no attack for the following six months. Dec. 22, 1920, at my request, she took a minute amount of mustard with her usual midday meal. As expected, this brought on a typical severe attack which lasted for almost a week. Since then over a year has elapsed with not a sign of any asthma. Her skin tests have remained unchanged.

Case 4.—A. Y., a Greek boy, aged 9 years, had had asthma since 5 years old. In the spring of 1920, when in this country only a few months, he developed pneumonia and empyema for which he was operated on at Mt. Sinai Hospital. Tuberculosis was at this time suspected. He came under my observation in November, 1920. His asthma was quite severe. There was a definite family history of both asthma and eczema on the paternal side. Eggs were said to cause the patient to become nauseated and vomit. He had generally enlarged lymph nodes, an enlarged liver and residual physical signs in his chest. A Pirquet test was markedly positive. Roentgenograms of the lungs showed definite areas of calcification in the enlarged paratracheal and bronchial nodes plus a marked hilus fibrosis and diffuse peribronchial thickening. His skin tests were strongly positive for egg (white and yolk), and chicken and less strongly for duck, goose and guinea fowl. Rigid abstinence from these foods in any form relieved only slightly. He was then given eight injections of egg-white, beginning with 0.1 c.c. of a 1:100,000 dilution (he gave a one plus reaction to the 1:10,000 dilution), and increasing every three or four days by 0.1 c.c. He felt much better during this period, but the eighth injection gave him such a severe general reaction, with typical asthma, that it was considered rather unsafe, with the lung involvement, to proceed further at that time and he was sent away to a tuberculosis hospital. He is improving very slowly but appreciably under a careful regime and dietary. He now gets an attack only at two to three week intervals. They last about twenty-four or thirty-six hours and go away leaving him without the continuous wheezing he formerly had. His skin tests have remained the same.

Case 5.—M. M., a colored girl, aged 10, who had suffered with asthma since the age of 5, was brought to the clinic by our social service nurse. The child was in such a weak condition that she could hardly stand up. Her dyspnea and orthopnea were extreme. She had a severe, dry, cracked eczema of the arms, chest and legs. Oatmeal was the only food that she was thought to have an idiosyncrasy to. An older sister had had asthma until she had gone South to college at the age of 18. Skin tests on the patient showed a marked sensitization to horse dander with a lesser reaction to pineapple, carrots and oats. On investigation, it was discovered that she lived immediately opposite the stables of Durland's Riding Academy. She was immediately sent to the country, where during six weeks she gained 9 pounds in weight and had no asthma whatsoever. Her skin was absolutely clear on the day she arrived home. That night she began to wheeze and the next day had a severe attack of asthma. Her skin again began to get rough and within a few days was as bad as ever. Injections of dilutions of horse dander were begun and improvement was soon very noticeable. When she was well enough, her tonsils, which were badly diseased, were removed. The skin condition has been held in check but never completely cured. The constant exposure to horse dander emanations continues to bring on attacks, although very mild in comparison. The parents have been unable to move up to the present. She could go to school with regularity soon after the injections had gotten under way and the mother was apparently satisfied to the extent that she did not like to keep the girl out of school for these injections and so they have been discontinued. The attacks come only once in every two to three weeks and are then only mild and last but a few hours.

Case 6.—M. H., a boy, aged 12, had had urticaria for ten summers and during the past two years had been getting attacks of bronchial asthma. He had had eczema when 1 year old. His skin tests were all negative as to any food sensitization, but he gave a two plus reaction to corn pollen. Injections of increasing doses of corn pollen dilutions (prepared by the Arlington Chemical Company of Yonkers) were given to the patient, in all about ten injections. That summer he had only a very mild attack of urticaria and none at all the following summer (1921). He has had no asthmatic attacks since this treatment was given.

Case 7.—I. N., a boy, aged 13, had had asthma, the same all year round, since 4 years of age. His attacks came on especially at night. There was nc history of eczema or urticaria. His father's father and a maternal grand-aunt had asthma. The patient's tonsils and adenoids were very badly diseased. Skin tests revealed a strongly positive reaction to rabbit hair and doubtful reactions to a few easily eliminated foods. A pillow he was using contained rabbit hair and he gave a positive reaction to an alkaline extract of this hair. Removing his tonsils and adenoids and changing his pillow effected an absolute cure. He has had no asthma in the eight months since then, although he had several colds.

CASE 8.—J. W., an Irish boy, aged 3, had been suffering from asthma for fourteen months when he came to the clinic. Six months previously his tonsils and adenoids had been removed and this had given him some relief. He still got attacks every few weeks, sometimes very severe ones. His tests showed a sensitization to both chicken feathers and goose feathers. A feather pillow he was using was discarded and a pine pillow substituted, and since then—a period of fifteen months—he has been entirely free of asthma.

CASE 9.—R. G., a girl, aged 18 months, had suffered with spells of difficult breathing and coughing since 6 months of age. An aunt had pulmonary tuberculosis and had come in contact with the child on occasional visits to the home. Examination revealed typical asthmatic breathing and musical râles, but nothing else. The child's nutrition was excellent. Skin tests showed no sensitizations. A Pirquet test was very strongly positive. Roentgenograms of the chest showed two adjacent areas of infiltration in the right lower lobe, the larger shadow being about the size of a quarter dollar. The child ran a temperature of about 100 to 100.5 F. in the evenings for a few weeks, but under good home care (the mother had been a trained nurse) this disappeared, as did the asthmatic symptoms after a month or so, without any but symptomatic treatment. She has not had a return of the condition in over a year now. Her Pirquet test remains the same. Roentgenograms show the lesions slowly getting smaller, although still present six months ago. The child's robust state of nutrition throughout was very interesting.

ECZEMA CASES

CASE 10.—E. A., a girl, aged 4½ years, had had an eczema since the second week of life. At the onset it was a typical infantile eczema which improved and grew worse from time to time but never cleared up entirely. Since 1 year of age it had become much more aggravated and chronic. It was generalized and the skin became thick and firm. She had been told on many occasions that nothing could be done for it. The family history was not suggestive of any anaphylactic conditions. The mother did not know any foods to which the child might have an idiosyncrasy. The skin looked exactly as does a case of mild ichthyosis, but she had itching which is not usually present in that condition. The dry thickened condition of the skin with the deep furrows and cracks gave her face the appearance of that of an old woman.

A Wassermann test on her blood was negative. Skin tests were performed on her chest and abdomen where the skin was least changed and very many positive reactions were secured with the control test being negative. The following were her reactions: three plus to banana and ovomucoid; two plus to short ragweed, egg-white, potato, bean, lima bean, mustard, and a fresh sample of some home-cooked peaches which were suspected because of a doubtful reaction to the stock preparation of peach; one plus to egg-yolk, pineapple, shad, and egg plant; doubtful reactions were secured to thirteen or fourteen foods, among which were wheat and lactalbumin. The prognosis was naturally poor. As rigid a diet as possible was prescribed and injections of egg-white were begun. The first dose was 0.05 c.c. of a 1:100,000 dilution of egg-white. This dose had to be increased very slowly and carefully because of the itching and aggravation which an increased amount often set up. As the patient lived out of town, the treatments could be given but once a week. The improvement has been very great. Her entire trunk, neck, arms, and thighs are as smooth and soft as most normal children's. She occasionally scratches her back when an injection has caused itching. Her face has cleared up remarkably. On several occasions in the past two to three months it was absolutely clear and smooth, but then the dry scaliness reappears for a few days—never very marked—and goes away again. The lesions on her hands, forearms, and knees persist more stubbornly but look very much better than at the onset of treatment. For a period of two months, hypodermic treatment was stopped and mouth desensitization was attempted, but with poor results. After this period, the skin reactions to egg-white were as markedly positive as at the beginning of treatment, so that the dose had to be materially cut down again, almost to where we began at first. It is my intention to give her additional injections of ragweed protein this spring to see if improvement will be any more rapid or complete.

Case 11.—M. C., a female colored child, aged 14 months, had had eczema since her sixth month. Her face, scalp, and buttocks were involved, and the lesions were of the red, moist, exudative variety. The family history was negative as to syphilis or anaphylaxis. Skin tests were all negative. Wassermann and Pirquet tests were negative as was a roentgenogram of the lungs. The mother's Wassermann test was negative. Local treatment helped very slightly. The lesions on the forehead became hypertrophic and assumed a keloid-like appearance. The buttocks cleared up very slowly. When last seen, at 2 years, the eruption on the forehead was still present.

This is the sort of case, I believe, for which roentgen-ray treatment may have done some good. I present it here to show a case in which the skin tests did not help at all.

Case 12.—A. F., a girl, aged 22 months, had had eczema since four months of age. When first seen it was of a mild, dry seborrheic and papular variety, on the face, arms and buttocks. The mother had had eczema and urticaria in her childhood, and throughout her family were similar histories. Her skin tests gave two plus reactions to eggs and milk, and one plus to rye and wheat leucosin and proteose, with doubtful reactions to corn, barley, oats, potato, and wheat globulin and glutenin, and coffee. Her control test was negative. It is interesting to note that her parents owned a bakery and lived in the rear. A cereal-free diet with only one pint of boiled milk and no eggs was attempted as closely as possible. The child was taken at about this time to live with her grandmother in Long Island City and I did not see her again for a year. She was absolutely free of all eruption which had cleared up fairly rapidly on the diet and while away from home. In the preceding few months her diet had gradually been made more liberal, adding one cereal after another and then foods with egg in them until at the time when I saw her again she was eating almost everything. Her skin tests, at this time, instead of being negative as expected, were the same as they had been. This is an interesting example, in my opinion, of a so-called latent sensitization in which the amount ingested is not enough to give her symptoms. She apparently has become somewhat desensitized so that she may eat ordinary amounts of these foods without the return of the eczema.

CLINICAL DEPARTMENT

A CASE OF MYELOID CHLOROMA*

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Cases of chloroma are sufficiently rare to warrant reports of individual cases, particularly if of the myeloid variety, as the literature shows they are of less frequent occurrence than the lymphatic form.

REPORT OF CASE

History.—K. F., a boy, aged 18 months, the youngest child of three, born of healthy American parents, breast fed, was always well, except for an intestinal indigestion with diarrhea at 10 months, a double otitis media at 14 months, and an acute digestive disturbance at 17 months due to indiscretions in diet.

Aug. 30, 1919, the child was brought to the Clinic because of extreme irritability, restlessness at night, puffiness about the eyes and a swelling which had appeared on the left side of the head between the eye and the ear. Examination showed in addition, an enlarged gland at the angle of the jaw on the left side. There was a slight digestive disturbance.

Sept. 11, 1919, the weight was 10,810 gm., with a ptosis of the lid on both sides (the right worse than the left). A tumor was also manifest for the first time on the glabella and over the right zygomatic process.

September 17, the temperature was normal. The white blood count was 81,600 and the differential count showed 88 per cent. myeloblasts, myelocytes, micromyelocytes and degenerated forms, the remainder of the nucleated cells being a few nucleated red cells, small lymphocytes and polymorphonuclear neutrophils. The Wassermann was negative.

Urine: The urine was repeatedly negative.

At this time a diagnosis of myeloid chloroma was made, based on the blood findings and the tumor formations characteristically found on the calvarium.

Physical Examination.—Sept. 17, 1919. The tumors between the eyes and the ears on both sides have decreased in size somewhat; both softer than when last seen. On the left side it is 3 by 2.5 cm. in size; slightly raised. The right side is a little more prominent, the swelling extending from the eye to the ear, about 3 cm. in vertical diameter. Both eyes are bloodshot. The right eye nearly closed by the "drop" lid. Venules dilated on both sides. A tumor is also found in the right cheek, about the size of a walnut, and somewhat flattened in shape. Another is found on the left cheek, about the size of a hazelnut. There are no other tumors on the head aside from those mentioned. The skin shows ecchymotic spots on the left side of the abdomen; also an ecchymosis in the left cheek, 2 cm. in diameter, said by the parents to have followed an injury; this, however, is doubtful. The abdomen is flaccid. The liver edge 5 cm. below the margin of the ribs, in the right nipple line. The spleen is 2.5 cm. below the margin of the ribs, in the left anterior axillary line. Weight, 11,335 gm. In the right inguinal region there was a group of enlarged lymph glands, collectively about the size of a pigeon's egg.

The day following the child had a convulsion, became comatose, and died. On this day another blood count was taken: 68,400 leukocytes, 2,800,000 erythrocytes, and the hemoglobin 70 per cent.

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* Received for publication, Nov. 8, 1921.

* From the Duluth Clinic.

NECROPSY FINDINGS

The necropsy was performed, Sept. 18, 1919, five hours after death.

Macroscopic.—The body was that of a well nourished male infant, 75 cm. in length and weighing 11,300 gm. The head circumference (fronto-occipital) measured 44 cm., the abdominal 47 cm., and the chest 47 cm. The skin was pale and mottled and showed postmortem lividity over the posterior part of the thorax. Rigor mortis was present in moderate degree. The hair was scant and dry. The scalp showed a slight seborrhea sicca. The anterior fontanel was open. The eyelids were swollen and the conjunctivae showed injection and ecchymosis, which was more marked on the right.

There was a tumor over each zygoma, having a firm consistency and the size of a hazelnut; tumors, somewhat larger in size and of a softer consistency, were present in each cheek, anterior to the parotid glands. Similar tumor masses were also present in the right submaxillary and the right submental regions.

Abdomen: The subcuticular fat was of normal thickness, consistency and color. The peritoneum was smooth, moist and shining. There was no fluid in the abdominal cavity.

The liver was moderately enlarged, the anterior edge being 4 cm. below the costal margin in the midclavicular line. On section it appeared normal in consistency and color. The gallbladder was somewhat thickened. The spleen measured 3 by 5 by 7.5 cm., and on section showed a firm and fairly fibrous surface. There were numerous adhesions between the anterior surface of the stomach and the transverse colon. The omentum immediately around these adhesions was thickened and studded with numerous small nodules. The pancreas was normal in size, but had a consistency somewhat firmer than normal. The left kidney measnred 3 by 4 by 4 by 8 cm. The capsule stripped easily, revealing a smooth surface. On section there were found to be numerous small nodules, similar to those seen in the omentum, scattered through the kidney substance. There were also small circumscribed pus pockets in the medulla. The markings were fairly distinct. The right kidney was of the same size and on section revealed a marked pyonephrosis, which had obliterated some of the pyramids. Nodules and pus pockets, similar to those seen in the left kidney, were present in both the cortex and medulla. These varied in size from a pinhead to a hazelnut. The ureters were 1 cm. in diameter and were thickened. Their external snrfaces were studded with small nodular tumors. The mesentery was greatly thickened and freely studded with small nodules, the largest approximating the size of a hazelnut. The stomach, intestines and urinary bladder showed no changes.

Thorax: The costochondral articulations were not enlarged but on the inner surface of the right sixth rib near the costochondral articulation was a small tumor measuring 0.75 by 1 by 1 cm. in size. There were no pleural adhesions and the lungs appeared to be normal macroscopically, except for a few airless areas. A large amount of turbid fluid, containing numerous white particles, was in the pericardial cavity. An irregular and lobulated tumor the size of a walnut, was found in the pericardium, extending upward from the diaphragmatic surface. The heart was normal in size and the valves were normal. The myocardium and epicardium contained innumerable small tumors, similar to those found in the kidneys.

Cranium: Section of the scalp showed the muscles to be pale. The scalp was easily removed except over the glabella, where a tumor, 1 by 2.5 by 2.5 cm. in size, and involving the periosteum was found. The anterior fontanel was 2 cm. in diameter. The dura was firmly adherent to the skull cap underneath the tumor and in this region the meninges were slightly thickened, and the brain injected. On section the brain substance appeared to be normal. The choroid plexus showed miliary tumors throughout. The spinal cord was negative.

Microscopic Study.—Microscopic sections of the tumors, taken from different parts of the body, show a more or less constant picture, varying somewhat, dependent on the character of the tissues infiltrated.

Kidneys: The section shows an area of kidney tissue almost entirely replaced by masses of tumor cells. These masses do not have a sharp line of demarcation, as seen in carcinoma, and show no tendency to any definite arrangement, although here and there circular configurations or rows of cells might suggest attempt at aciniformation. The cells are supported by a delicate fibrous network. The cells are practically all mononuclear, varying somewhat in size, and having round, triangular or quadrangular contours. The nuclei are relatively large, occupying one third to one half of the cell area; they are rich in chromatin and deep staining. The cytoplasm takes a rather deep eosin stain. In certain areas cells show degenerative changes, as evidenced by nuclear disintegration. Blood vessels are difficult to identify and simply suggest spaces between the cells. The tubules and some of the glomeruli are atrophied to a slight degree.

Liver: Section shows small masses of tumor cells having the same histologic characteristics and invasive tendencies as those seen in the kidney section. Some of the cells, however, are larger and show evidence of karyolysis.

Heart: The muscle fibers are separated by masses of tumor cells, exactly similar to those described in the kidney section. The invasion of tumor cells is very extensive.

Lungs: Sections through the airless areas, described above, show some of the alveoli filled with serum; while others, especially around the relatively larger arterial branches, contain cells histologically similar to the tumor cells in the kidney. Some of these infiltrate the alveolar walls.

Sections of lymph glands and the tumor masses over the glabella and the zygomatic processes showed pictures exactly similar to those described in the kidney section.

HISTORY AND REVIEW OF LITERATURE

It has always been a mooted question as to whether chloroma and the acute leukemias are definitely related in their pathogenesis, and authorities have aligned themselves on one side or another.

The first description of a case in the literature is by Allen Burns,[1] an American, in 1823. The name "chloroma," however, was first used by King,[2] of Glasgow, in 1853, antedating by one year, Aran[3] who is usually recognized as the author of the name. Aran himself recognized King as the first to use the term, but strangely enough, King does not mention the name "chloroma" in his paper, except in the title, which led Dock to infer that the name was known previous to the publication of King's article, at least in a conversational way. The first comprehensive study of the reported cases was in 1893, by Dock,[4] who collected seventeen cases including his own—but since then reports have been more frequent, and now more than 100 cases have been reported. All the early cases were considered to be of the lymphatic type, and it was not until the twentieth century that the myeloid type was described, when Roman[5] first collected the cases in the literature corresponding to the latter type. A better understanding of hematopoietic function is probably the reason for this more frequent recognition of the presumably less frequent myeloid form, as since then the proportion of myeloid cases has been fairly large, leading to the assumption that these cases were previously unrecognized, just as we now know that acute myelogenous leukemia is more frequently present than is ordinarily supposed.

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[1] Burns: Observations on the Surgical Anatomy of the Head and Neck. 1823.

[2] King: London & Edinburgh Monthly J. M. Sc. **17:** (Aug.) 1853.

[3] Aran: Arch. gén. de Méd., October, 1854.

[4] Dock: Am. J. M. Sc. **106**:211, 1893.

[5] Roman: Beitr. z. path. Anat. u. z. allg. Path. **55**:61.

Cause and Symptoms with Differential Features.—The symptomatology of the acute leukemias and the chloromas is similar in nearly every regard. Lehndorff[6] mentions the predilection of the tumor growths for the bones of the head and orbit in chloroma as a distinguishing feature of this condition. Practically all observers agree in this, and add as further differential points the distinctive color of the tumors postmortem, except in the fulminating cases. The course, clinical symptomatology, blood picture and termination, are the same. The consensus of opinion is that both are due to primary bone marrow disease, and that the infiltration into the tissues is more extensive in chloroma. The latter is more distinctly heterotopic, and its infiltration into heterotopic tissues is a characteristic. Threadgold[7] considers the infiltration of vessel walls and the surrounding connective tissue typical of chloroma, indicating a greater degree of malignancy.

The differentiation from acute leukemia is not the only obstacle in the diagnosis, as other conditions are frequently simulated. This is true of such clinical entities as lymphosarcoma, Hodgkin's disease, Sternberg's leukosarcomatosis, the so-called "nodular" leukemia and epinephroma. In contrast to lymphosarcoma and Hodgkin's disease, we have the distinctive blood picture, which in these two conditions is never so markedly altered. Gumbel[8] mentions the more marked, regular disposition of the cells in sarcoma as another factor. In Hodgkin's disease there is a slower course, with the absence of involvement of the parenchymal organs of the body and the usually nearly normal blood picture. Of the allied sarcomatous conditions, the disease known as epinephroma simulates chloroma most closely. It is characterized by metastases about the head and face, but is primarily an affection of the suprarenal glands, and the blood picture is aleukemic. Differentiation between leukosarcomatosis, nodular leukemia and chloroma is more difficult, and they probably are all merely variants of acute leukemic processes. Differentiation is made increasingly difficult when we consider the fine lines drawn in the interpretation of the cells found in blood smears. The cell frequently predominating in these cases is the so-called "lymphoid" cell, which resembles very closely the large lymphocytes found in the normal blood. Pappenheim[9] describes a cell of this type as the mother cell of all white blood cells. This cell is normally present in the foetus in the marrow of bone, the spleen, the liver and the lymph glands, but does not persist in adult life. He believes that in fetal life this cell has the power, probably through two varying factors, to develop either into a lymphocyte or a leukocyte.

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[6] Lehndorff: Jahrb. f. Kinderh. u. phys. Erziehung, July, 1910.

[7] Treadgold: Quart. J. M. **1**:239, 1908.

[8] Gumbel: Virchows Arch. f. path. Anat. **171**: 1903.

Ward[10] and other observers conclude that these large cells in the leukemic processes are a reversion to the primitive mother cell, which has this potentiality to form lymphocytes or myelocytes, according to the exciting factors predominating. This unknown factor is the agent which predetermines a myelogenous or a lymphatic type of acute leukemia. This is borne out by the fact that in myeloid chloroma or in acute myelogenous leukemia one finds all graduations from the mother cell to the myeloblast, the myelocyte and, finally, the adult polymorphonuclear cell. Ward claims that the considerations of the tissues affected in the pathology are inadequate grounds for classifying leukemias, as we know that obviously myeloid tissue may be found in the marrow, since these mother cells, by virtue of their presence in lymph glands, may, paradoxical as it may seem, form myelocytes, and in the bone marrow, lymphoyctes. Both sorts of tissue may be found in the tumors of chloroma, one or the other predominating. The clinical course and gross pathology of myeloid or lymphatic chloroma, as in acute leukemia, must, therefore, be solely made from the blood picture and from the microscopic sections of the tissue. When these large lymphoid cells are present in predominating numbers, one cannot conclude that the case is of the lymphatic type merely on account of this finding, and if myelocytes are present to any degree, the diagnosis of the myeloid form of leukemia is proper. The more forcible the stimulus to overproduction of the cells, the more primitive the cell type, and the more difficult the differentiation. We have an analogous response in the erythroblastic formation, produced by varying degrees of hemolysis. Likewise, in carcinoma, at times the parent tissue is reproduced, whereas in more rapidly growing epitheliomas the character of the cells may be of an indifferent type. It must be borne in mind, however, that acute cases, from the beginning, are, during their course, always permanently lymphocytic or myelocytic, and a metamorphosis of the cells does not take place after the process has once begun. In the more slowly progressive cases, the differentiation is less difficult, and aside from the blood findings, sections of the spleen frequently show myeloid cells in the splenic pulp, definitely displacing the lymph adenoid tissue of the malpighian corpuscles.

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[9] Pappenheim: Folia Hematol., 1904-1909.

[10] Ward: Proc. Roy. Soc. Med., Lond. **7**: 1914.

The Winkler-Schultz oxidase reaction is positive in these myeloid cases. Figure 1 shows clearly the predominating type of cells, distinctly myelocytic. Other cells, without granules, are present, undoubtedly myeloblasts and presumably lymphoid cells. The small number of adult cells, both lymphocytic and polymorphonuclear, is striking.

The blood picture in chloroma simulates or is identical with that of acute leukemia. Erythrocytes are oftentimes materially reduced, so that we may have less than one million per cubic millimeter. The hemoglobin is correspondingly reduced. The leukocytes vary in number from a leukopenia, as in Lehndorff's[6] case, he reporting only 5,100, to counts of 300,000 or more per c.m. The acuteness of the process usually may be identified by the incidence of the large lymphoid cells. The percentage of myelocytes in our case is unusually large. Turk[11] reported 44 per cent. myelocytes, whereas ours showed 77 per cent.

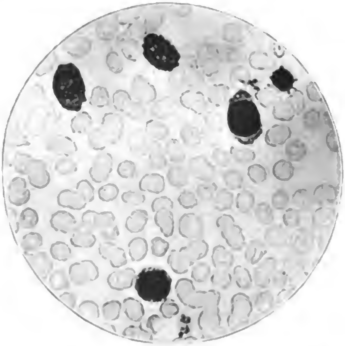

Fig. 1.—Photomicrograph of the blood smear, showing the myelocytes under high magnification.

A feature in our case not definitely explicable is the preponderance of myelocytes over the large, indeterminate lymphoid cells, in view of the fact that our patient lived only four weeks—a more rapid course than we have noted in any case previously reported.

Aside from the pathogenesis of the disease, another interesting feature is the green color which is almost invariably found in the chloromatous tumors. Quite a few cases, however, have been reported, in which this green color was not present; for example, those of Birk,[12]

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[11] Turk: Wien. klin. Wchnschr., 1902.

[12] Birk: St. Petersb. med. Wchnschr. **7**:377, 1883.

Leber,[13] Wende,[14] Miller [15] and ours. Observers have noticed that the more fulminating the case the less apt the green color is to be present. As an example, Miller's case is cited, the patient living only three months. Our case ran its course in one-third that time. Furthermore, the green color is oftentimes absent in many of the tumors, and greenish discoloration has been noticed in lymphatic tuberculosis and in ordinary leukemias. The cause of the color is unknown. The color usually does not appear except postmortem, but has been seen at operation. Paviot [16] discovered that the color spontaneously fades on exposure to the air, and reappears when treated with ammonia or peroxide of hydrogen.

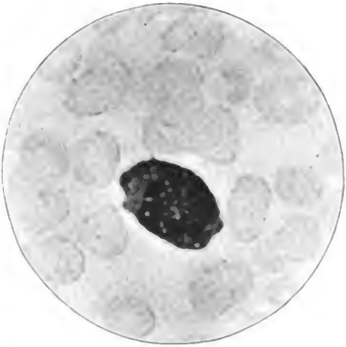

Fig. 2.—Photomicrograph of an individual myelocyte under still higher magnification.

Some of the older theories regarding the distinctive color found in chloroma are those of Balfour,[17] who believed that the pigment was a bilirubin derivative, and of Dittrich,[18] who thought it was a premature putrefactive change. Reynolds [19] thought a combination of fatty acids with iron was the factor. Huber [20] and Chiari [21] believed the pigment to be a lipochrome. They stated that they saw fatty greenish granula-

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13. Leber: Arch. f. Ophth. **24**:295.
14. Wende: Am. J. M. Sc., 1901, p. 836.
15. Miller: Arch. Path. Inst., Lond. Hosp. **1**:1.
16. Paviot and Fayolle: Prov. méd., 1897.
17. Balfour: Edinburgh M. & S. J. **43**:319, 1835.
18. Dittrich: Prag. Vierteljahrsschr. f. d. prakt. Heilk. **2**:104, 1846.
19. Pope and Reynolds: Lancet **1**:1351, 1907.
20. Huber: Arch. d. Heilk. **19**: 1878.
21. Chiari: Prag. Ztschr. f. Heilk. **4**: 1883.

tions in chloroma tissue, but the majority of writers have not been able to corroborate this. Askanazy[22] points out the fact that fat is pigmentophil, and thinks that the pigment is merely incorporated in the fat goblets. The parasitic theory has been advanced by Lang, but no one has ever been able to isolate any organisms except such as occasionally are implanted secondarily. Virchow and von Recklinghausen[23] have attributed the color to the so-called parenchyma color typical of chloromatous tumors, just as we have typical parenchyma colors in the liver, myocardium, etc. The color is presumed to be merely due to the physical effect produced by the molecular structures of the tissues. Askanazy[22] promulgated the theory that the color in chloroma is analogous to the color found in pus. He has been able to bring out the same color change in pus as in chloroma by treating it with a mixture of formalin and ammonia. He thinks that cells of the myeloid series are necessary for the production of this green color, as the oxidation of lymphocytes gave no green reaction, except in a case of malignant lymphoma which was found to be rich in eosinophils. He also suggests that the less highly differentiated cells frequently found in the rapidly fulminating cases of chloroma are not so apt to produce this change, myelocytes and myeloblasts causing it more distinctly. This was not the experience in our case; in spite of the high percentage of myelocytes and myeloblasts there was nothing to suggest a greenish tinge, but merely a grayish discoloration. None of these theories has been proved, and a great many are not capable of proof, and the subject is still debatable.

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22. Askanazy: Internat. Clinics, 1913.

23. Von Recklinghausen: Tageblatt der 58ten Versammlung deutscher Naturforscher und Aerzte in Strassburg, 1885.

PROGRESS IN PEDIATRICS

THE ALLERGIC OR HYPERSENSITIVE CONDITION

A REVIEW OF TWO YEARS' PROGRESS *

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An essential advance in the understanding of anaphylaxis and related phenomena, which occurred early in this period of two years, has been the restrictive definition of the term "anaphylaxis." For the classification of the various conditions which were thereby excluded and which had hitherto been regarded as manifestations of anaphylaxis, the terms "allergy" and "hypersensitiveness" are now in general use. The hypersensitive condition, according to Coca,[1] is one of specific or particular reactivity, with characteristic symptoms, to the administration of or contact with, any substance in a quantity which, to most of the individuals of the same species is innocuous. In amplification he adds: (1) "The characteristic symptoms are generally different in the different animal species for the same group of substances." (2) "They are uniform in any one species for various substances." (3) "Where the exciting agent possesses a normal physiological action; for example, the drugs, the symptoms of this action are, with few exceptions, different from those of hypersensitiveness to that agent." This excludes the tuberculin reaction because its symptoms are the same for all species and the so-called "toxin hypersensitiveness" because the symptoms are not different from those of the normal physiological effect of the agent.

The phenomena of true hypersensitiveness, Coca says, are those of anaphylaxis and those of allergy.

Anaphylaxis is defined by the same author as hypersensitiveness induced and experimental, not inheritable, and due to the presence of specific antibodies in certain tissues.

Allergy, on the other hand, is a natural inherited condition of hypersensitiveness which affects only human beings and is not dependent in any way on immunologic antibodies. Coca and other authorities are not, however, in complete accord as to the relation of specific antibodies to allergic phenomena.

Coca points out, furthermore, that if true anaphylaxis ever does occur in man, it does so very rarely, and he believes that there is no positive evidence that it occurs at all in human beings. The allergic

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* Received for publication, June 20, 1922.

[1] Coca: J. Immunol. **5**:363, 1920.

phenomena to which some of us are subject would, therefore, be independent of artificial sensitization and often, in fact, occur at first contact without opportunity for sensitization to have taken place in the ordinary meaning of the word.

According to Wells[2] the criteria for true anaphylaxis are:

> (*a*) The observed toxicity of injected material must depend upon the sensitization of the animal; i. e., must not produce similar symptoms in non-sensitized animals.
>
> (*b*) The symptoms produced must be those characteristic of anaphylactic intoxication, and therefore the same for all antigens with the same test animal, but differing characteristically with each species.
>
> (*c*) It should be possible to demonstrate passive sensitization with the serum of sensitized animals.
>
> (*d*) It should be possible to demonstrate typical reactions in a strip from the virgin guinea-pig uterus.
>
> (*e*) It should be possible to demonstrate amelioration or prevention of the bronchial spasm in guinea-pigs by the proper use of atropin and epinephrin.
>
> (*f*) The possibility that the observed symptoms are caused by capillary thrombosis or embolism must be excluded.
>
> (*g*) After recovery from anaphylactic shock there should be exhibited a condition of desensitization under proper conditions.

Wells also states that there is no satisfactory proof that anything except proteins can act as anaphylactogens (antigens of anaphylactic reactions). The only soluble proteins as yet found not to be antigenic are those which are, from the chemical sense, incomplete proteins, and there is evidence that lack of certain amino-acids may be the essential deficiency. Solubility is essential since, although insoluble proteins may eventually be brought into solution in the animal body, the process is too slow to bring about anaphylactic reactions, and is probably also accompanied by a disintegration of the protein molecule. Heating to a degree that does not disintegrate the proteins affects them only to the extent that it makes them insoluble. Among the few proteins not made insoluble by heating are casein and ovomucoid, and these are antigenic despite boiling.

There is disagreement and doubt as to the true nature of serum disease allergy in relation to anaphylaxis. Drug hypersensitiveness seems undoubtedly a distinct phenomenon. Schloss[3] has been able to transfer sensitization to guinea-pigs by the injection of serum from patients in four cases, and Ramirez[4] reports an interesting case which appears as an example of passive sensitization to horse dander from man to man by transfusion of 600 c.c. of blood. Coca, however, feels that the evidence is not conclusive in this case, that the transfused patient was not already allergic toward dander and has found in addition that the same donor previously gave 800 c.c. of blood to another patient in whom no symptoms of sensitization appeared.

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2. Wells: Physiol. Rev. **1**:44, 1921.
3. Schloss: Am. J. Dis. Child. **19**:433 (June) 1920.
4. Ramirez: J. A. M. A. **73**:589 (Sept. 27) 1919.

Zinsser,[5] in determining the relation of the tuberculin reaction to anaphylaxis, states that in guinea-pigs two fundamentally different types of intradermal reactions can be produced; one immediate and transitory, which develops in animals sensitized against proteins and is true anaphylaxis; and one, the tuberculin type, which develops more slowly, leads to more profound injury of tissues, and is independent of anaphylaxis. Tuberculin sensitization is easily accomplished only with live infections, and reactions follow intradermal injections of extracts of bacteria from which all coagulable proteins, nucleoproteins and Bence-Jones bodies have been removed as far as possible by boiling with acid. Anaphylactic sensitization developed by injections of dead bacterial material is not as quickly developed as tuberculin sensitization. Manifestations of tuberculin sensitiveness also differ in animals and man from those characteristic of anaphylaxis in each species.

Attempting to produce tuberculin sensitiveness with constituents of dead bacteria, Zinsser has obtained hopeful results only with massive injections, and these of substances precipitated with acid.

Fleishner, Meyer and Shaw[6] have shown by experiment that bacterial proteins, whether insoluble or soluble, which sensitize guinea-pigs in an anaphylactic sense will not sensitize its skin. The observations of Auer[7] on the effect of independent local irritants are of interest in this connection. He determined that xylol, when applied to the ears of nonsensitized rabbits, produced no very marked amount of inflammation. If sensitized animals were used, however, the application of this substance, when followed by the injection of otherwise ineffective amounts of the antigen to which the animals were sensitized, caused necrosis. He concluded that this result was due to the accumulation of effective amounts of antigen in the treated area, owing to the inflammatory reaction initiated by the xylol. This suggests a possible relation between drug idiosyncrasy and anaphylaxis.

It does not seem desirable to include in this review references to the literature on anaphylaxis except as they may be directly enlightening to the understanding and treatment of allergy and hypersensitiveness in man. For further information on anaphylaxis one may examine the comprehensive and authoritative treatises by Besredka,[8] Coca[9] and Bordet.[10]

It appears that the nature of anaphylaxis and the understanding of its mechanism is comparatively well established but that the nature of the allergic or hypersensitive condition in man is more elusive to the understanding and possibly much more complex in its mechanism. As a rule, according to Longcope,[11] the symptoms in man appear early in life and may be observed the first time the patient comes in contact with the substance to which he is hypersensitive. There is undoubtedly a definite tendency toward the inheritance, not of specific hypersensitiveness, but of a quality of tissue that allows of the development of idiosyncrasies. This may be dependent on the condition of the body fluids or of the cells, which permits of a ready union of foreign protein with them. A striking peculiarity of these patients is that the skin reacts by the formation of an urticarial wheal, to the application of the substance or substances to which they are sensitive.

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[5] Zinsser: J. Exper. M. **34**:495, 1921.

[6] Fleishner, Meyer and Shaw: Am. J. Dis. Child. **18**:577 (Dec.) 1919.

[7] Auer: Proc. Soc. Exper. Biol. & M. **17**:93, 1919.

[8] Besredka: Anaphylaxis and Antianaphylaxis and Experimental Foundations, C. V. Mosby, 1920, p. 156.

[9] Coca: Tice, Practice of Medicine, New York, W. Pryor Company, 1920, p. 107.

[10] Bordet: Bull. Johns Hopkins Hosp. **32**:269, 1921.

Turnbull [12] believes that sensitization may be acquired during intercurrent disease, or overexertion or worry, or by the absorption of bacterial products from foci, or by over eating or repeated eating of certain foods, or by the ingestion of certain foods too soon after illness or exhaustion. In some persons there may have been a combination of one or more of these circumstances.

The Cutaneous Reaction.—It is remarkable that in contrast to the thousands of cases reported in American medical literature, virtually no activity in the determination of the incidence of the cutaneous reaction is discoverable elsewhere. Furthermore, correspondingly little specific treatment appears to be given. Most foreign reports on the treatment of asthma and of "alimentary anaphylaxis" indicate that the injection or ingestion of peptones or other nonspecific substances is the more favored method.

Either the cutaneous or the intracutaneous method may be used for testing. Schloss [3] in a comparison of the two methods, prefers the cutaneous method. His study was made on 100 infants and children not apparently suffering from disturbances due to food and on thirty who suffered definitely from this cause. His conclusions were that the intracutaneous test is more sensitive but more misleading owing to its tendency to cause pseudoreactions. Many vegetable proteins are difficult to obtain in any form soluble in physiologic sodium chlorid solution, but are soluble only in alkaline solvents and thus cannot be used intradermally. To insure sterility, the proteins used for the intradermal test solutions must be carefully prepared, which adds considerable technical difficulty. On two occasions he has seen severe infections due to such tests. Another objection is that a very sensitive patient may be made seriously ill by the injection of even a minute amount of the protein to which he reacts.

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11. Longcope: J. A. M. A. **77**:1535 (Nov. 12) 1921.
12. Turnbull: Boston M. & S. J. **182**:497, 1920.

The greatest limitations of the cutaneous test, according to Schloss, are that it is not conclusive when negative. This deficiency, he suggests, may be due to lack of skin sensitization, or, possibly to temporary desensitization.

In these opinions Schloss is in agreement with Walker and a large number of other authors; nevertheless there are and have always been those who are vigorous supporters of the intracutaneous method. Larsen, Paddock and Alexander [13] favor the intracutaneous test because it is more delicate; the dry preparations are too uncertain, and they can do more tests in less time and with less trouble. They find, however, that the solutions for the intracutaneous tests are apt to show a precipitate after a while, and lose their potency. They also find that certain points on the body, particularly the fold at the elbow, are more favorable than others to the development of a reaction.

Brown,[14] commenting on Walker's selection of the cutaneous method, questions the value of his experiments with intracutaneous applications because of the use of too much fluid in the injections and because his standard for a normal reaction allowed of too many positive reactions. Using a fluid preparation prepared according to Coca's method in seventy-eight cases, he claims the superiority of the intracutaneous method on the following grounds: (1) every case known to be clinically sensitive to a protein gave a reaction. (2) The scratch method with dry powdered proteins gave positive reactions in only 50 per cent. of the cases, and with his more potent fluid preparations, in only 80 per cent. (3) The intradermal method is not so painful nor so disfiguring. (4) The intradermal method requires less time for application and for obtaining results, which is an important advantage in office-work. (5) The same preparation can be used conveniently for treating and testing. (6) General reactions occasionally follow the dermal scratch application as well as the intradermal injection.

Cooke,[15] writing on the danger of constitutional reactions from dermal and intradermal tests, reports one death following an intradermal test injection containing not more than 0.002 mg. of nitrogen. He refers to one instance of constitutional reaction following the scratch method of testing, and reports several in his own experience from the intracutaneous injection. Such cases have been reported by Park [16] and by Gerstenberger and Davis.[17] Cooke suggests that there is special danger of provoking these reactions when changing from a weak preparation to a strong one. When a constitutional

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13. Larsen, Paddock and Alexander: J. Immunol. **7**:81, 1922.
14. Brown: J. Immunol. **7**:97, 1922.
15. Cooke: J. Immunol. **7**:119, 1922.
16. Park: Am. J. Dis. Child. **19**:46 (Jan.) 1920.
17. Gerstenberger and Davis: J. A. M. A. **76**:721 (March 12) 1921.

reaction is diagnosed, Cooke recommends, first, the application of a tourniquet to restrict, if possible, the rate of absorption of the injection; secondly, the injection of epinephrin in strong doses—from 0.4 to 0.6 c.c. in children and 1 c.c. in adults, either subcutaneously or intravenously according to the severity of symptoms. This should be repeated after a short interval if symptoms continue to progress and, in his experience, is not dangerous. There may also be indications for the use of strophanthus intravenously, up to 1 mg.

The reports quoted indicate an apparent superiority amounting to about 20 per cent. in favor of the delicacy of the intradermal method of testing, which is or is not offset by the greater liability to constitutional reactions, according to personal opinion. The inference is clear, however, that the protein preparations used by these authors may be especially potent. The method of preparing these proteins was devised by Coca and is explained in his paper on the subject.[18] Vander Veer,[19] testing the comparative potency of four of the best known commercial preparations of proteins, and that obtained from the Department of Applied Immunology of the New York Hospital, known as the "Cornell preparation" (Coca's method), found that none of the commercial preparations even approximated the potency of the strongest Cornell preparation. The strongest or most potent of these seemed about equal in potency to a medium strength Cornell preparation containing 0.005 mg. of nitrogen per c.c. All preparations were in the fluid form and tests were made by the ophthalmic method. They state that experience indicates that for therapeutic effects a maximum potency is desirable but that in using these preparations more caution is necessary in order to avoid constitutional reactions.

Mackenzie and Baldwin,[20] experimenting to determine the exhaustibility of the skin reaction after repeated reactions on the same site, conclude: (1) that in persons manifesting a cutaneous reaction, the reactivity of the skin may be locally abolished by repeated applications to the same area; (2) The reactivity of the skin at the exhausted site may not return for three days or longer. (3) The exhaustion appears to be specific and is not apparent when some other substance is used. (4) The extent of the area of exhaustion is strictly limited to the site of the reaction. (5) Nonspecific cutaneous reactions produced by nonantigenic substances such as histamin are not only inexhaustible but progressively increase with each repetition of the application to the same site. (6) From these results they suggest the possibility of genuine local desensitization and suggest its application in the treatment of hay fever and allergic rhinitis. Larsen, Paddock and Alexander [13]

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18. Coca: J. Immunol. **7**:163, 1922.
19. Vander Veer: J. Immunol. **7**:113, 1922.
20. Mackenzie and Baldwin: Arch. Int. Med. **28**:722 (Nov.) 1921.

attempted to confirm these results by repeated injections in two persons at intervals of one hour. With this technic nine intracutaneous injections in one person and four in the other in the same skin area failed to abolish the reaction of the skin. After the eighth injection, the first patient had symptoms of hay-fever, and his eighth and ninth reactions were locally the largest and his arm became much swollen. The next day a typical reaction was obtained again on the same site. When tests were made at intervals of one week, however, these two cases showed a definitely decreased reactivity, the duration of which was not accurately tested, but at the end of three weeks the reaction was again produced as strongly as ever. Their experiments, therefore, are partially confirmatory to those of Mackenzie and Baldwin.

Desensitization and "Hyposensitization".—Cooke,[21] comparing diminished sensitization in allergic conditions in man with desensitization in experimental anaphylaxis, believes that the uniform failure to induce complete insensitiveness in allergy indicates that the relative insensitiveness is of a nature different from that of desensitization in anaphylaxis. He proposes that this distinction he made by designating such a modification of allergic sensitiveness "hyposensitization." He has studied the phenomena of "local exhaustion" of the allergic cutaneous reaction described by MacKenzie and Baldwin, and finds in disagreement with these authors that the exhaustion is nonspecific.

Incidence of the Cutaneous Reaction.—That evidence of sensitization can be obtained by the cutaneous or scratch method in patients whose history is free from the consequences of such sensitization is shown by Baker [22] and by Peshkin and Rost.[23] Baker obtained ten positive and eleven doubtful reactions in twenty-five children whose history indicated no allergic conditions. In comparison with these he reports fifty-five positive and fifty-three doubtful reactions in seventy-four children with symptoms of a probable allergic nature. Peshkin and Rost tested 502 children who were carefully selected as giving in their histories no symptoms which could be attributed to allergy. They report positive reactions in only five, all of whom were more than 5 years of age. They also contained sixty-seven doubtful reactions The total number of tests done on these 502 children was 9,406, an average of only nineteen per patient. Baker concludes that the incidence of sensitization in apparently normal children is almost negligible, but unless his ten positive reactions were all obtained from one or two of his twenty-five normals, one can hardly agree with this estimate. Peshkin and Rost conclude that 10 per cent of apparently normal children show doubtful or positive reactions which decrease as their age

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21. Cooke: J. Immunol. **7**:219, 1922.
22. Baker: Am. J. Dis. Child. **19**:114 (Feb.) 1920.
23. Peshkin and Rost: Am. J. Dis. Child. **23**:51 (Jan.) 1922.

increases, indicating progressive desensitization. On the basis of their own figures, especially in consideration of the small average number of tests, this percentage seems too conservative. Baker's tests were confined to food proteins.

The articles of diet found by Baker to be most commonly the source of allergic symptoms were in the order mentioned: oatmeal, potato, egg, peas, rice, casein, beef juice and chicken.

Rackemann[24] reports the results of cutaneous tests in 939 patients presenting various clinical conditions. He obtained positive reactions in about 100 cases in which nothing compatible with this reaction appeared in the history. Subsequently, in following these patients, thirteen developed conditions in relation to which the reaction obtained proved important.

Of 118 cases of hay-fever and pollen asthma, forty-eight gave reactions to proteins other than pollens. Of forty-five cases of horse asthma, fifteen gave positive results with other proteins. Of thirty-one cases of dust asthma, there were many complicating reactions. Of nineteen cases of food asthma, four gave numerous reactions to other proteins. Of 156 bacterial asthmas, 103 with fairly complete skin tests showed positive reactions to other proteins. It is desirable, according to Rackemann, to make a wide variety of tests and to so limit the patients' life and habits that they will come in contact only with negatively reacting proteins. Positive reactions, however, should not be taken very seriously unless compatible with the patient's history, or if further study proves their importance as etiological agents.

Coca[25] states that the age incidence of natural allergies increases rapidly in the early age periods but probably does not greatly exceed 10 per cent. in any period. Coca, Deibert and Menger[26] find that the American Indian is apparently much less frequently affected by the allergies than is the white race.

Sensitization in Hay-Fever.—In this disorder skin sensitization is so nearly universally present that although tests are useful as confirmatory evidence and, as Walker suggests, to determine the strength of immunizing doses, it is, perhaps, more essential to know the usual offending pollens, their regional distribution, and their season of pollination. There are, however, cases in which symptoms are perennial rather than seasonal.

The frequent causes of perennial hay-fever, according to Walker[27] are animal emanations, particularly dander and cat hair, ingested foods, inhaled cereal grains, and sometimes pollens, these last being usually relieved by the ordinary preseason treatment. Recurring head colds are sometimes due to sensitization which renders the nasal mucous membrane more irritable. Nonsensitive patients with perennial hay-fever, provided there are no demonstrable abnormalities, growths, and the like in the nasal cavities or sinuses, are sometimes benefited or relieved by autogenous vaccines from nasal secretions. A pseudo hay-fever caused by mechanical, thermal or odorific irritants is not uncommon.

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[24] Rackemann: Am. J. M. Sc. **163**:87, 1922.

[25] Coca: J. Immunol. **7**:193, 1922.

[26] Coca, Deibert and Menger: J. Immunol. **7**:201, 1922.

[27] Walker: J. A. M. A. **75**:782 (Sept. 18) 1920.

Of seasonal hay-fever in New England the dwarf ragweed is practically always the cause of late symptoms—in August and September, and timothy causes 90 per cent of the early cases of hay-fever, in June and July. Rose and redtop occasionally cause early hay-fever and when their season happens unusually early it may interfere with the course of treatment.

Watson and Kibler[28] have investigated the etiology of hay-fever in Arizona and the Southwest. They find that of the wind pollinated flora of these regions the artemisias, or wormwoods, have little, if any, importance. Amaranths are an important factor and their pollen is very active. As a predominating cause of hay-fever in the Southwest they take the place of ragweed in the east and the artemisias in the Rocky Mountains. In some seasons *Atriplex wrightii* will probably take the place of *Amaranthus palmeri*. *Capriola dactylon* (Bermuda grass), causing spring, summer and fall types, will probably prove to be the common grass causing hay-fever at altitudes up to 4,500 feet, and *Poa pratensis* (June grass) above that altitude.

Gaertneria dactylon (rabbit bush) and *Atriplex canescens* (shad scale) are probably the most important plants causing the spring type of hay-fever. Trees are probably not an important cause, but when they do cause hay-fever it will be of a very early type, and the most important are cottonwoods and the ash. The principle of group reactions is not applicable to hay-fever in Arizona and the Southwest.

Heredity in Hay-Fever.—Scheppegrell,[29] investigating the incidence of heredity in 1000 cases of hay-fever, found that 358 patients had relatives of the first degree who also suffered from hay-fever. In view of the heterogeneous nature of the heredity reported in other allergic conditions, the fact that the hypersensitiveness should be manifested in the same way in so many cases seems especially remarkable.

Results and Methods of Treatment of Hay-Fever.—Most of the reported cases of hay-fever have been treated by the preseasonal immunization process of Walker, that is, by the injection of increasing doses of the specific pollen protein, beginning considerably before the season of pollination and being completed shortly previous to the opening of the season. There is unanimity of opinion that the specific protein must be used in order to obtain success rather than the preparations of mixed pollen proteins distributed by commercial houses.[30] These are open to the same criticism that is justly leveled at mixed vaccines or "shot-gun" drug prescriptions. Scheppegrell [31] finds that some cases do not give a marked skin reaction while others do. In the first group the dose of protein may safely be increased rapidly and it is necessary to reach a much higher number of units in order to be effective. In the strongly reacting group, the dosage should be increased cautiously but treatment should be given as intensively as possible.[32]

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[28] Watson and Kibler: J. A. M. A. **78**:719 (March 11) 1922.

[29] Scheppegrell: Med. Rec. **98**:216, 1920.

In view of reports previously quoted of the greater potency of certain protein solutions, particularly the Cornell preparations of Coca, it seems advisable that all such solutions or dry proteins should be compared with some suitable standard before using.

That treatment during the hay-fever season cannot be given with as much chance of success is indicated by Williams,[33] who reported that twenty-seven cases due to ragweed were not benefited by treatment after the onset of symptoms. Of five cases due to goldenrod, there resulted some benefit in two and much improvement in one. Walker [34] reported, however, that 32 per cent. of twenty-two grass pollen hay-fever patients were made practically free from symptoms by treatment given during the season; 18 per cent. more were benefited to the extent of 75 per cent.; 13 per cent. were 50 per cent benefited; and 13 per cent. were 25 per cent benefited. Of twenty-seven cases due to ragweed, 14 per cent. were made free from symptoms, or practically so; 11 per cent. were 75 per cent. improved; 25 per cent. were 50 per cent benefited, and 44 per cent. were not benefited. He adds that bacterial vaccine treatment during the season occasionally seems to be beneficial. Late preseasonal treatment gives better results than treatment during the season.

Rackemann,[35] reporting the results of preseasonal treatment, found that 9 per cent. of ninety-one patients with fall ragweed hay-fever were made entirely free from symptoms; 62 per cent. were considerably relieved. The best results were obtained by moderate amounts of specific treatment since even after more considerable preparation the tolerance for regweed remained at a very low level. Systemic reactions occur after 2 per cent. of injections and are not always due to an overdose. Hay-fever, he believes, depends on a mechanism which is not anaphylactic, but which is perhaps closely related to that of drug idiosyncrasies.

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[30] Editorial, J. A. M. A. **77**:791 (March 19) 1921.

[31] Scheppegrell: Med. Rec. **100**:191, 1921.

[32] Caulfield: J. A. M. A. **76**:1071 (April 16) 1921.

[33] Williams: Mil. Surg. **46**:199, 1920.

[34] Walker: Arch. Int. Med. **28**:71 (July) 1921.

[35] Rackemann: Boston M. & S. J. **182**:295, 1920.

Walker[34] finds that preseasonal treatment with ragweed pollen was the cause of complete freedom in 22 per cent. of 202 patients; 30 per cent. more were benefited at least 75 per cent.; more than 23 per cent. were only 50 per cent. improved, and 6 per cent. were not benefited at all. Of fifty-two patients whose hay-fever was due to grass pollens, 40 per cent. became free from symptoms; more than 17 per cent. were made practically free; 19 per cent. were 75 per cent. benefited; 17 per cent. were 50 per cent. benefited, and about 6 per cent. were not improved.

For seventy-three patients having ragweed hay-fever who received the preseasonal treatment two years in succession, Walker gives the following figures:

	First Year, Per Cent.	Second Year, Per Cent.
Symptom free	38	16
Practically free	22	22
75 per cent. benefited	19	45
50 per cent. benefited	16	12
Not benefited	6	4

He believes the poorer results obtained the second year in the first group were due to the fact that these patients were apt to get less treatment. He believes that the greater amounts of preseasonal treatment give the better results.

Caulfield,[31] with a small group of thirteen fully treated patients, that is, receiving at least 0.05 c.c. of 1:5 dilution, found that all were very much improved. Walter[36] finds that preseasonal inoculation against ragweed has not helped his cases, while in hay-fever due to rose, timothy, daisy, etc., there has been success. He believes that ragweed hay-fever is a different problem and suggests alkaline therapy and fractional doses of the pollen during the season.

The most interesting divergence from the subcutaneous method of immunizing is that MacKenzie[37] who, having in previous experiments with Baldwin[20] observed the exhaustion of local skin reactivity following repeated applications of specific protein to the same area in a sensitive subject, attempted to exhaust the reactivity of the nasal membranes by the instillation of pollen solutions. He quotes Dsergowsky[38] and Blumenau[39] as producing an active immunity by applications of diphtheria toxin to the mucosa of the nose, throat and trachea, and Ehrlich on the production of immunity by applications of the

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36. Walter: J. A. M. A. **75**:670 (Sept. 4) 1920.
37. Mackenzie: J. A. M. A. **78**:787 (March 18) 1922.
38. Dsergowsky: Ztschr. f. Immunol. **2**:602, 1910.
39. Blumenau: Ztschr. f. Immunol. **3**:196, 1911.

antigens ricin and abrin to the upper air passages or to the alimentary tract. He also quotes Sewall and Powell [40] who obtained either sensitization or immunization in guinea-pigs, depending on the dosage, by intranasal instillation.

In his report eight patients were treated by subcutaneous injections only; twenty by local applications only, and twenty by combined methods. His results were:

	Injections	Spray	Both
Complete relief	0	1	3
Almost complete	3	2	9
Considerable	4	6	6
No relief	1	1	2

Although the number of cases was unfortunately very small, the use of the spray in this manner combined with treatment by injections seems attractive.

Sensitization in Asthma.—Unfortunately, the large numbers of cases which Caulfield [31] and Sanford [41] have reported are not so grouped that asthma cases can be separated from those of hay-fever. In Sanford's report 100 cases, presumably asthmatics, reacted to one or more of the proteins derived from foods, particularly to egg white, to which eleven patients reacted. To proteins of various grains, twenty-five persons reacted, and twenty-eight reacted to vegetable proteins, but these twenty-eight were, on the whole, negative to the therapeutic test. Fruits had apparently little to do with his cases of asthma, although banana, which produced several positive reactions, was twice shown to ba a causative agent. In 365 tests with preparations of *Staphylococcus pyogenes aureus* and *S. pyogenes albus* there was not a single reaction. Caulfield also found bacterial skin tests consistently negative and has virtually discarded these proteins in his tests. The experiments, previously mentioned, of Fleishner, Meyer and Shaw are of interest in this connection. Rackemann,[42] however, reports somewhat differently concerning their importance: In forty cases of asthma, he isolated from the sputum 129 different organisms on blood agar. These consisted of: 72 nonhemolytic streptococci, or 60 per cent.; 17 hemolytic streptococci, or 13 per cent.; 17 staphylococcus albus, or 13 per cent.; 7 gram-negative cocci; 5 staphylococcus aureus; 3 pneumococci; 2 gram-negative bacillus; 1 diphtheroid bacilli; 11 others. The percentages, according to Rackemann, would vary with different technic and with mice passages the pneumococci would have been more prominent.

Intradermal tests with proteins from these were done on thirty-nine patients to whom they were autogenous, and twenty-five gave positive skin tests. Some gave reactions to heterologous preparations and in all, out of fifty-six patients, thirty-four gave positive reactions.

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[40] Sewall and Powell: J. Exper. Med. **24**:69, 1916.

[41] Sanford: Minnesota Med. **3**:180, 1920.

[42] Rackemann: J. Immunol. **5**:373, 1920

Treatment was successful in fairly close accordance with the positive tests, ten patients treated with injections of a positively reacting autogenous protein were benefited. It was also true that four out of six treated with positively reacting heterologous preparations were benefited. No negatively reacting patients were improved.

Rackemann concludes that asthma due to bacteria depends on a condition of specific cellular sensitiveness, either to the bacteria themselves or to the products of their action in the body. Caulfield, on the other hand, feels that the failure of vaccine therapy is sufficiently marked in contrast to protein therapy to cause one to question that both are etiologic agents acting in a comparable fashion. Cooke [43] questions the specific value of vaccines in allergy and has failed to find proof that bacterial extracts will act as allergens. He, therefore, does not make the diagnosis of bacterial asthma. For some of these cases he believes that dusts are responsible, and names particularly hay dust and house dust as containing specific nitrogenous factors.

Coke [44] mentions, among other interesting instances of sensitization, certain married patients who are hypersensitive to human hair and whose health is better when sleeping apart. This author, using the scratch tests for diagnosis, finds that 50 per cent. of all asthmatics and 90 per cent. of asthmatic children give reactions. These percentages seem very high in consideration of the extensive reports by American authors. He also concludes that much can be done for nonreacting cases by nonspecific protein therapy.

Pines [45] reviewing 150 cases of asthma, concludes that it is due to protein sensitization and that it is possible with cutaneous tests to determine the etiology in about 50 per cent. of the cases. Cunningham [46] tested thirty-six children with asthma, found positive reactions in eleven, or 30 per cent., but was able to confirm this relationship in only six, or 17 per cent.

Other Causes of Asthma.—Gerdon [47] discusses his experiences with asthma in fur dye workers. The dyes used were ursol dyes, and derivatives of p-phenyldiamin. There seemed to be a distinct relation between the asthma and exposure to this dye and in addition patients suffered from salivation, edema, diarrhea and exopthalmos. Asthma would sometimes recur at the mere odor of the dye. He believes that the indications in these cases point to sensitization.

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43. Cooke: J. Immunol. **7**:147, 1922.
44. Coke: Brit. M. J. **1**:372, 1921.
45. Pines: California State M. J. **19**:29, 1921.
46. Cunningham: Boston M. & S. J. **186**:876, 1922.
47. Gerdon: Zentralbl. f. Gewerbehygiene **8**:201, 1920.

Sluder[48] considers that in some cases asthma may be the result of a nasal reflex and mentions six examples. Knapp[49] believes the disease to be due to insufficiency of the pylorus with long continued pressure of the diaphragm against the lungs. The remarkable case reported by Ramirez, which was apparently due to passive sensitization by transfusion, has already been mentioned.

Pathology of Asthma.—Kamchorn and Ellis[50] report the necropsy findings in an additional case of death from asthma, making two such cases in their own experience, and review the reports of ten similar cases reported by other observers. They conclude that the histology of the bronchi shows simply acute catarrhal bronchitis and does not explain the course of bronchial asthma. The length of time a person suffers from the disease and the number of attacks he has are apparently without effect on the bronchi (The patient reported on had had asthma all his life). The theory of spasm is favored by these findings. In addition to the bronchial findings the cases showed hypertrophy and dilatation of the heart.

Treatment of Bronchial Asthma.—This may be considered first from the specific standpoint, including the diagnosis of protein sensitization and consequent elimination of the indicated proteins, or the diagnosis of an infectious etiology and treatment by immunization. It is the general opinion, and Caulfield states that the results of elimination of allergic substances surpass in promptitude and completeness the results of other methods of treatment.

Hutcheson and Budd[51] treated ninety asthmatics with autogenous vaccines and by removal of diseased foci. Most of the cases were chronic. In fifty-three, or 75 per cent., either complete freedom from attacks or the longest interval of freedom since the disease began was obtained. In the remainder there was no improvement. Walker has previously reported considerable success from the use of autogenous vaccines. Cunningham[46] obtained relief in seven of twenty children so treated. Rackemann's results from the use of autogenous, positively reacting bacterial proteins has already been mentioned.

Gottlieb[52] reported the relief of symptoms in fifteen of thirty-two asthmatics by the elimination of positively reacting proteins. In a second paper[53] he recommends the use of bacterial vaccines prepared from the stools. He reports one case of colon bacillus allergy and states, furthermore, that in hay-fever and asthma, the normal intestinal

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48. Sluder: J. A. M. A. **73**:589 (Sept. 27) 1919.
49. Knapp: Med. Rec. **101**:55, 1921.
50. Kamchorn and Ellis: Am. J. M. Sc. **161**:525, 1921.
51. Hutcheson and Budd: Virginia M. Month. **46**:281, 1919.
52. Gottlieb: J. A. M. A. **75**:814 (Sept. 18) 1920.
53. Gottlieb: J. A. M. A. **74**:931 (April 3) 1920.

flora is often replaced by the predominance of unusual bacteria for these locations, which indicates an intestinal disturbance probably of bacterial origin. This may play a part in the etiology.

Auld[54] in the most recent of several papers on the use of non-specific protein therapy, reports very successful results. He uses injections of Witte's peptone. The patients ought always to be placed in the best possible surroundings and should have specific skin tests before attempting this form of treatment. Cunningham[46] has had good results from a change of climate and believes that for asthmatic children residing in our Atlantic coast cities particularly, the removal inland is indicated when the cause seems to be bacterial.

Sensitization in Eczema.—Fox and Fisher,[55] in sixty cases of eczema in adults, found nineteen giving positive reactions. O'Keefe[56, 57] found that 35 per cent. of 131 bottle fed babies and older children showed sensitization to one or more of the common food proteins. In the order of frequency these foods are egg, milk, potato, wheat and oat. In these cases also, fat or carbohydrate indigestion was more often found than would be the case in an unselected group of children. He suggests that these forms of indigestion make protein sensitization more likely to occur and so produce eczema.

In forty-one exclusively breast fed babies having eczema, he was surprised to find that more than 60 per cent. showed sensitization; 40 per cent. of these being sensitive to egg, 39 per cent. to cow's milk, 5 per cent. to oat, and about 2 per cent. to wheat. None showed a reaction to human milk protein. The conclusion is that human milk must often contain foreign proteins which the babies may absorb in an unbroken form, thus becoming sensitized. The treatment of removing such positively reacting foods from the mothers' diets, together with external remedies, resulted in a cure in seventeen of forty-one treated. Whenever milk or eggs were so limited or omitted, cod liver oil and green vegetables were especially prescribed.

In bottle fed babies those sensitive to casein were fed with whey and cream mixtures. Those sensitive to lactalbumin received milk prepared by boiling and skimming off the coagulated material; for those sensitive to both casein and lactalbumin, the formulae were peptonized or were restricted to the minimum in protein. In nearly 20 per cent. of the seventy cases reported in the first of these two papers there was evidence of heredity.

Sidlick and Knowles,[58] using the intracutaneous method of testing, found that of twenty-five children with eczema, fifteen gave positive

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54. Auld: Brit. M. J. **1**:696, 1921.
55. Fox and Fisher: J. A. M. A. **75**:907 (Oct. 2) 1920.
56. O'Keefe: Boston M. & S. J. **183**:569, 1920.
57. O'Keefe: J. A. M. A. **78**:483 (Feb. 18) 1922.
58. Sidlick and Knowles: Am. J. Dis. Child. **23**:316 (April) 1922.

reactions. Of these fifteen, six were either cured or much improved by the removal of the reacting proteins. Of twelve cases with papular eczema, nine reacted to one or more proteins and seven of these patients were either cured or very much improved. We assume that external treatment was also employed. Engman and Wander[59] found skin reactions in 78 per cent. of thirty-six cases of infantile eczema and in every instance where control could be exercised got excellent results from the indicated treatment.

Schloss,[3] in fifty-three cases of infantile eczema, found forty giving cutaneous reactions, thirty-four to egg white which had never been eaten but which nevertheless produced symptoms. Thirty-six gave reactions to cow's milk, and although it was difficult to omit this food at this age, six were fed on an artificial milk and, by the the improvement in their eczema, confirmed the indicated etiology of milk protein. Schloss feels that infantile eczema is also often due to the fat or sugar in the food.

In a second group consisting of twenty-four children more than 16 months of age, ten gave positive reactions. In these the type of eczema was rather definite, the patients showing a dry, scaly skin, with weeping areas occurring only in periods of marked exacerbation. The distribution in these cases usually included the hands, forearms, bends of the elbows, and the popliteal spaces. Six of them reacted to so many proteins that therapeutic confirmation of the relation of any one of them was impossible. The remaining four were greatly improved when the protein indicated was removed.

Schloss' figures for children of all ages would show 65 per cent. giving positive cutaneous (scratch) tests. Sidlick and Knowles tested thirty-five children, using the intracutaneous method, and 68 per cent. reacted. With the scratch method in 131 children O'Keefe had only 35 per cent. positives.

The infantile cases of Schloss and of Engman and Wander gave positive reactions in about 77 per cent. of eighty-nine children. O'Keefe's group of breast fed babies, numbering forty-one, were 60 per cent. positive. Allowing for O'Keefe's uniformly lower results, it would appear that breast fed babies may give positive skin tests as often as the bottle fed.

Sensitization in Other Skin Diseases.—Engman and Wander,[59] in ten cases of urticaria, found positive skin reactions in 79 per cent. In chronic general eczema (distinguished from infantile eczema) 38 per cent. of twenty-one patients gave skin reactions. The percentage of reactions was almost negligible in eleven cases of dermatitis herpetiformis, six of erythema multiforme, four lichen urticarius, two of pemphigus, and three of purpura hemorrhagica. Acne vulgaris was negative in eighteen cases, and two others, which were slightly positive, did not respond to specific treatment. Schloss,[3] in sixty children with urticaria, found only ten giving skin reactions, and only four of these were helped by the indicated treatment. The same negligible results were obtained in angioneuritic edema and erythema multiforme. Three cases of acute dermatitis all proved to be due to pollens.

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[59] Engman and Wander: Arch. Dermat. & Syph. **3**:223 (April) 1921.

Spain,[60] investigating the nature of ivy poisoning or dermatitis venenata, concludes that typical vesicular lesions can be produced by alcoholic or chloroform extracts of fresh leaves of *Toxicodendron* radicans applied to the skin surface. Such lesions could not be produced by the intradermal injection of the extract, thus indicating that poisoning is not due to allergic sensitization. The age incidence of susceptibility to this irritant is indicated by the fact that 65 per cent. of persons more than 8 years old are susceptible, whereas no reaction could be produced in eighteen infants.

Allergy, Serum Disease and Dermatitis Venenata.—Coca [25] draws the following comparisons: (*a*) Serum disease differs from other forms of human sensitization in the almost constant period of incubation and the high incidence of susceptibility. (*b*) Dermatitis venenata differs from other forms of human hypersensitiveness in which the skin is affected by the constant and characteristic nature of the lesion. (*c*) The age incidence of natural allergies increases rapidly in the early age periods but probably does not greatly exceed 10 per cent. in any period. (*d*) The age incidence of dermatitis venenata increases greatly from childhood to adult life and reaches a very high percentage—probably 90 per cent. (*e*) The age incidence of serum disease seems not to change during life.

Serum Disease.—Gurd and Roberts [61] report a fatal case resulting from the injection of antitetanic horse serum. Kraus et al.,[62] and Krause [63] recommend the use of bovine serum instead of horse serum as a vehicle for diphtheria, tetanus, or other antitoxins, on the ground that it is less liable to cause serum sickness.

Bouche and Huston,[64] studying the reactions in man to from 0.5 to 2 c.c. of horse serum subcutaneously, conclude that both the local and general reactions vary in different persons. There is usually a vascular or sympathetic reaction at first, followed by a trophic or autonomic reaction, and the manifestations of the two phases are those seen in anaphylactic shock.

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60. Spain: J. Immunol. **7**:179, 1922.
61. Gurd and Roberts: Lancet **1**:763, 1920.
62. Kraus et al.: München. med. Wchnschr. **68**:1244, 1921.
63. Krause: Rev. d. Inst. Bact. **2**:1, 1919.
64. Bouche and Huston: Presse méd. **29**:801, 1921.

Davidson[65] finds that the rashes of serum disease differ in relative frequency and in the order of occurrence, the order in either respect being urticarial, morbilliform and circinate. He suggests the possibility of a distinct mechanism for each. The most important symptoms accompanying such rashes are pyrexia, joint pains, edema, adenitis, and increased cardiac dulness.

Cowie and Greenthal[66] found that normal horse serum always protects guinea-pigs against lethal doses of diphtheria toxin if injected in sufficient quantity and question the superior value of serum from immunized horses.

Lewis[67] believes that the rate of absorption of subcutaneously injected serum or protein solutions is so slow that even when the site of the injection is massaged it could not account for the cases of sudden death occasionally reported. By intravenous injection, on the other hand, animal experiments indicate that extremely small amounts of antigenic protein will bring on fatal anaphylactic spasms. It is by the accidental entering of small veins, therefore, that Lewis accounts for these fatalities in human beings. Cook[68] mentions influences increasing or delaying the rate of absorption.

MacRenzie and Leake,[69] in studies on nineteen patients injected with foreign serum, conclude that their results support the antigen-antibody conception of serum disease.

Intestinal Allergy.—The surprising results of skin tests in exclusively breast-fed babies reported by O'Keefe, 60 per cent. of whom showed positive reactions to proteins other than those of human milk, have been mentioned. The sensitizing capacity of human milk thereby suggested is also pointed out by Shannon.[70] In this report the author mentions three cases, one each of urticaria, indigestion, and papular eczema, all being in nursing babies. In each case he was able to demonstrate by the anaphylactic reaction that egg protein had passed into the mothers' milk. All three babies were relieved of symptoms after the mothers had omitted egg from their diets. In one baby the skin test for egg yolk was positive.

Schloss[3] presents experiments showing that the ingestion of foreign protein, both milk and egg, by guinea-pigs causes the development of immune reactions. Furthermore, Grulee and Bonar[71] examined 136 specimens of urine from twenty-five infants selected only in being from 1 to 13 days old. These babies differed from controls in that they received egg albumin water between feedings instead of plain water. Of the twenty-five test cases, eighteen showed a positive precipitin reaction to egg white in their urines at some time during these thirteen days of life. From seventeen control babies, forty-one urines gave no positive reactions. These results indicate that the intestinal wall of the new-born infant from the fourth to the tenth day, inclusive, is permeable to egg white in quantities sufficient to be determined by the precipitin reaction in the urine. It seems likely that this is not a peculiarity of specific cases but is a general characteristic of this period of life and suggests an explanation of the frequent sensitization to egg and other foreign proteins. In a previous paper,[72] Grulee had determined that egg albumin is usually completely broken down by the digestive processes in infants and children, as indicated by the infrequency with which he had obtained positive precipitin reactions to this substance in the stools.

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[65] Davidson: Glasgow M. J. **92**:20, 1919.

[66] Cowie and Greenthal: J. M. Research **41**:261, 1919.

[67] Lewis: J. A. M. A. **76**:1342 (May 14) 1921.

[68] Cook: J. Immunol. **5**:39, 1920.

[69] MacKenzie and Leake: J. Exper. M. **33**:601, 1921.

[70] Shannon: Am. J. Dis. Child. **22**:223 (Sept.) 1921.

[71] Grulee and Bonar: Am. J. Dis. Child. **21**:89 (Jan.) 1921.

Zubizarreta [73] believes that the feeding of cow's milk to babies sensitizes them occasionally against cow's lymph and so accounts for the cases sometimes seen of severe disturbances following vaccination. Wells and Osborne [74] isolated four chemically distinct proteins from cow's milk by the use of the anaphylactic reaction in guinea-pigs. These are casein, lactalbumin, lactoglobulin, and an alcohol soluble protein. Lactalbumin and serum globulin appear to be chemically indistinct and produce mutual sensitization in guinea-pigs.

Duke [75] mentions six cases of abdominal pain apparently the result of food allergy. He believes that food allergy is observed more frequently in persons who have had lesions of the gastro-intestinal tract than in normal persons. Zubizarreta [73] believes that if food is not completely "homologized" in the upper intestinal tract it is likely to produce sensitization. He also believes that eggs are more easily digested after being kept for a while, and is in favor of extracts of the stomach or of upper intestinal tissues rich in the ferments of digestion and "homologization" or of peptone or of beef extract given in 0.5 gm. doses one half hour before meals as an anti-anaphylactic.

Schloss [8] states that the usual gastro-intestinal disturbances consist of vomiting and diarrhea; that infants showing these symptoms acutely, together with urticaria and edema, always give a cutaneous reaction to cow's milk protein and their symptoms occur after the ingestion of very small amounts of milk. In another group symptoms are less acute and may not occur until the milk has been taken for several days. These rarely show positive reactions to cow's milk, but that the conditions may, nevertheless, be caused by protein sensitization is indicated by the good results of feeding boiled or evaporated milk and by the fact that infants suffering from identical symptoms may show positive reactions to milk protein. Immunity to certain foods can be developed by the ingestion of graduated doses. In twenty cases of cyclic vomiting he found only two giving positive skin tests. Blackfan [76] believes that the absolute omission of offending foods may be unnecessary, since some patients can tolerate them in small quantities. A high temperature is, in his experience, apt to prevent these disturbances. He considers desensitization by all means the most satisfactory method of procedure, and feels that in young infants and children this is best done by mouth rather than by subcutaneous injection. Cunningham [46] feels that by the omission of these foods for varying periods sensitization often disappears spontaneously, and for this reason recommends postponing artificial measures of desensitization when possible until it is determined after two or three months that this will not occur. Park [16] mentions an interesting case of food allergy resulting in the spontaneous disappearance of the hypersensitive condition.

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[72] Grulee: Am. J. Dis. Child. **20**:15 (July) 1920.

[73] Zubizarreta: Semana méd., Buenos Aires **27**:513, 1921.

[74] Wells and Osborne: J. Infect. Dis. **29**:200 (Aug.) 1921.

[75] Duke: Arch. Int. Med. **28**:151 (Aug.) 1921.

Other Conditions Due to Allergy.—Pagniez and Leutand [77] refer to cases of epilepsy apparently due to sensitization, but base their diagnoses on the observed results of ingestion of or contact with the proteins, rather than on the results of skin tests.

Drug Idiosyncrasy.—Cooke [78] states that in fifteen cases of drug reactions a positive history of family hypersensitiveness occurred in twelve. In the remaining three cases the evidences of sensitization were multiple and included such conditions as asthma, urticaria, and hay-fever occurring in the same individual. Occasionally with the antipyretics hyperpyrexia occurs, or cardiac collapse. In virtually all cases there was a marked eosinophilia. Acetylsalicylic acid reactions were the most frequently encountered by this author. Symptoms begin in from fifteen to twenty minutes after the ingestion of 10 grains and may last from eight to thirty-six hours. Positive cutaneous reactions do not occur except in those cases giving a history of urticaria.

Cooke classes the types of drug action as follows: (*a*) Normal action—side action and toxic action. (*b*) Idiosyncrasic action—either exaggerated normal or exaggerated side action, or lessened normal action (tolerance). (*c*) Allergic action—abnormal.

Labbe and Haguenau [79] report a case of antipyrin sensitization, and Peshkin [80] cites one of ipecac idiosyncrasy with asthma.

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76. Blackfan: Am. J. M. Sc. **160**:341, 1920.

77. Pagniez and Lieutand: Presse méd. **27**:693, 1920.

78. Cooke: J. A. M. A. **73**:759, 1919.

79. Labbe and Hagenau: Bull. et mém. Soc. méd. d. hôp. de Paris **43**:549, 1921.

80. Peshkin: J. A. M. A. **75**:1133 (Oct. 23) 1920.

Lane[81] reports three cases of susceptibility to procain in dentists, confirming the diagnosis by skin tests, and suggests the possibility of general reactions to this substance.

Stuart and Maynard[82] report an interesting case of hypersensitiveness to arsphenamin following an exfoliative dermatitis which gave a marked intracutaneous skin reaction. They examined in this way ten other cases treated with arsphenamin and sixteen controls. No positive skin tests were found among the controls. Of the other ten cases, seven gave no reaction. Two patients gave positive reactions and had lumbar pain beginning four days after an injection of arsphenamin and lasting four weeks. The third patient exhibited the same lumbar pain following the last injection but gave no skin reaction, possibly because the most recent therapeutic dose had been given as long as nine months previously.

Nonspecific Treatment.—Most of this treatment is given either by mouth or intravenously. Commenting on the use of intravenous treatment, Hanzlik and Karsner[83] studied twenty-nine agents given in this way and concluded that they were distinctly harmful in varying degrees. They are, therefore, opposed to the promiscuous and unwarranted giving of drugs by the intravenous method.

Auld[54] has written several reports on the successful treatment of asthma with Witte's peptone given intravenously. Pagniez and Vallery-Radot[84] believe that "alimentary anaphylaxis" can be avoided by the preliminary injection of peptone. Van Leeuwen and Varekamp[85] tried specific skin tests but concluded that nonspecific injections (they use tuberculin) give better results. Shulman[86] reports good results in the treatment of sixty cases of arthritis, and especially arthritis of gonorrheal origin, by the injection of milk. Snyder and Ramirez,[87] reporting on seventy cases of chronic arthritis, conclude that such patients as have not been relieved by the routine treatment with salicylates, hot packs, baking, and massage, are, as a rule, materially benefited by the intravenous administration of small doses of foreign protein. Such benefit is almost always in the joints of the upper extremities. Patients prefer secondary proteoses to typhoid bacilli because they seem to cause less discomfort. The effects in relieving pain and improving motion seem equally good.

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[81] Lane: Arch. Dermat. & Syph. **3**:235 (April) 1921.

[82] Stuart and Maynard: Arch. Int. Med. **26**:511 (Oct.) 1920.

[83] Hanzlik and Karsner: J. Pharmacol. & Exper. Therap. **14**:379, 1920.

[84] Pagniez and Vallery-Radot: Ann. de méd. **8**:303, 1920.

[85] Van Leeuwen and Varekamp: Lancet **2**:1366, 1921.

[86] Shulman: Med. Rec. **98**:47, 1920.

[87] Snyder and Ramirez: Arch. Int. Med. **28**:50 (July) 1921.

Joltrain,[88] Zubizarreta,[73] and Nathan[89] favor treatment by preliminary ingestion of peptone or extracts of certain of the digestive tissues to prevent "alimentary anaphylaxis."

Danysz[90] reports further successes in the treatment of nonfebrile chronic diseases by means of cultures of nonpathogenic intestinal micro-organisms. His most effective preparations seem to contain strains of *Bacillus coli, B. proteus,* streptococcus, staphylococcus, and enterococcus. He differs the proportions for psoriasis, enteritis, asthma, etc. His reports may be compared with those of four other authors already quoted, Turnbull,[12] Larsen, Paddock and Alexander,[13] Cooke[43] and Gottlieb.[53]

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88. Joltrain: Bull. et mém. Soc. méd. d. hôp. de Paris **43**:556, 1921.
89. Nathan: Bull. méd., Par. **34**:59, 1920.
90. Danysz: Bull. méd., Par. **34**:657, 1920.

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THE AMOUNT OF BLOOD TO BE TRANSFUSED IN ANEMIA OF CHILDREN (BLOOD DOSAGE) *

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Rapidly as the advance in blood transfusion has taken place, and brilliant as the results have been, it must be admitted that some details have been more or less neglected.

A study of the literature shows that one of the simplest questions still remains unanswered, viz., the exact amount of blood to be transfused. It is very important that this be determined in every case as exactly as is possible; because if too much is given, danger of hypertransfusion becomes imminent; if too little is given, the result will be nil.

Until now no method has been known by means of which one could determine beforehand how much blood was needed to cause a definite increase in the number of red blood cells. Nor could one foretell the degree of increase after the transfusion of a known quantity of normal blood. In fact, the question of blood dosage is a very vague one. While one author advocates a dose for infants up to 150 c.c., another says that a safe limit is to give up to 15 c.c. for each pound of body weight.

It is evident that neither can be right; for it is clear that the amount will depend on more factors than age or weight alone. In the first place, the state of the patient's blood has to be considered. A child with 800,000 red blood cells will need more blood than one with 2,800,000 cells, both being anemic. Secondly, the weight of the patient is of importance; a newly born infant needs less blood than a full grown man. Thirdly, the desired result is a factor—the higher the blood counts desired, the more blood is needed. Fourthly, the kind of anemia is also a determining factor whether the blood forming organs are impaired functionally, or whether the spleen and other blood reservoirs are hyperfunctioning, or whether there is an hydremia, or an oligemia.

It is generally known that after transfusion the red blood cell values usually are increased. Investigators who have studied this effect, and who have tried to discover a constant rule in the changes following this

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procedure, always were discouraged by the fact that in certain cases the blood count showed the same values after transfusion as before, or were even found to be decreased. Their final conclusion was that the counts did not show any constant changes (Huck[1]). I wish to emphasize that in nearly all these cases the patient suffered from a serious disease of the blood forming organs (often there existed pernicious anemia) which distorted the results. In other cases in which this abnormal condition was not present, there can be found a constant change. I hope to prove in this paper that the change in the blood count is, in the main, parallel with (1) the body weight of the patient, and (2) the amount of blood transfused.

My interest in the question of blood dosage arose from observations made on two little patients with anemia that were transfused at Leiden in 1919, and who received the same amount of blood (500 c.c.). One of them, a boy, aged 4 years, weighing 13.75 kg., showed after transfusion of 500 c.c. an increase in the number of red blood cells from 1 million to 3.3 millions—an increase of 2.3 millions. The red blood cells of the other boy, aged 2½ years, weighing 11.5 kg., rose from 2.2 to 4.7 millions—an increase of 2.5 millions. These two boys, of nearly the same weight, showed after transfusion of an equal amount of blood a nearly equal rise in the number of red blood cells—the larger boy showing the smaller rise.

I received the impression that in these cases the two bloods had been mixed, just as though they had been mixed in a vessel outside the body, with the restriction that the volume after the procedure was reduced to the volume of the patient's blood before. I believe that the mechanism was as follows: After the blood of the donor has entered the patient's vessels, a dilatation of these vessels takes place and the two bloods are mixed. Within from twenty-four to forty-eight hours the vessels get back their original volume, and the blood bulk is reduced to the volume present before the transfusion, the surplus disappearing. In this volume now is circulating the sum of the recipient's corpuscles plus the corpuscles from the donor.

How many corpuscles has the patient now? To answer this question it is necessary to estimate the blood volume of the patient. We know that the number varies considerably, even in the same patient, and therefore, it cannot be determined with great accuracy. I believe it is possible to base an estimation on a figure approximating one thirteenth of the body weight (7 per cent.) of the patient. This keeps the average between the figures of Haldane and Smith[2] (1/20) and Lucas and Dearing[3] (14.7 per cent. = 1/7).

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[1] Huck: Johns Hopkins Hosp. Bull. **30**:63, 1919.

[2] Haldane and Smith: J. Physiol. **25**:330, 1900.

[3] Lucas and Dearing: Am. J. Dis. Child. **21**:96 (Jan.) 1921.

My argument at first was as follows: Supposing that a child weighing 13 kg. (containing 1 kg. of blood) needs to have the number of red blood cells raised from 1 million to 3 millions. This could be done by giving the number of red blood cells present in 1 kg. of blood with 2 millions of red blood cells, which equals 0.4 kg. of normal blood. We have to transfuse 0.4 liter, or 400 c.c. As such calculations proved to work out correctly, I formulated the problem as follows: How much of normal blood do we need for each kilogram of body weight to make the number of red blood cells increase one million?

Concurrence Between Observed Rise of Red Blood Cells and Theoretical Rise in Twenty Transfusions

No. of Case	Diagnosis	Weight in Kg.	Amount of Blood in C.c.	Red Blood Cells in Millions		Rise of Red Blood Cells in Millions	Theoretical Rise of Red Blood Cells in Millions
				Before Transfusion	After Transfusion		
1	Anemia, hypoplastic ?	13.75	500	1.0	3,3	2,3	2,4
2	Anemia, secondary	11.5	500	2,2	4,7	2,5	2,8
3	Von Jaksch (syphilis)	5.8	150	1,7	3.4	1,7	1.7
4	Von Jaksch (sepsis)	6.2	150	2,3	3,5	1,2	2 4
5	Anemia, secondary	7.11	300	1,5	3,9	2,5	2,8
6	Anemia, secondary	8.25	350	2.1	6,2	4.1	2,8
7	Von Jaksch	3.7	63	2,0	3,0	1,0	1,1
8*	Von Jaksch	3.8	85 ?	2,3	3.1	0,8	1,5
9	Anemia, secondary	10.7	170	2,4	3,6	1,2	1,5
10*	Anemia, secondary	9.7	175	3,7	4,7	1,0	1,2
11	Anemia, secondary	2.3	72	2,9	5,1	2,2	2,0
12	Anemia, secondary	6.28	250	1,2	4.7	3,5	2,7
13	Von Jaksch	4.55	130	2,6	4,4	1.8	1,8
14	Von Jaksch	8.5	160	3,4	4,6	1,2	1.3
15	Von Jaksch	5.77	180 ?	3,1	4,6	1,5	2,0
16	Anemia, secondary	19.5	380 ?	3,3	5,0	1,7	1.3
17	Anemia, secondary	7.62	230	1,6	3.6	2,0	2,0
18	Anemia, secondary	3.9	85	2 8	4,5	1,7	1.7
19	Anemia, secondary	7.9	150	3,9	4.3	1,4	1,3
20	Anemia, secondary	4.6	150	1,2	3,8	2,6	2,1

* Second transfusion in same patient.

Considering that each kilogram of a child contains 1/13 kilogram of blood, and supposing that normal blood contains 5 million red blood corpuscles, it is evident that this quantity will be $1/5 \times 1/13 \times 1{,}000$ c.c., or 15 c.c. per kilogram. Thus we come to the thesis: In cases of simple anemia in which we wish to make the red blood cells increase 1,000,000, we have to transfuse 15 c.c. per kilogram of body weight.

To prove this, I have put together in a table the blood counts of all patients who were transfused at the Leiden pediatric clinic and have compared the rise of their red blood cells with the theoretical rise. Beginning with about case 6 I have even used my method to fix the amount of blood to be transfused, and with rather good results.

It is obvious from this table that in most cases the number of red blood corpuscles nearly approached the estimated number. In only three cases was there any great difference.

In Case 4 the blood counts were too low, which may have been caused by the blood destruction that resulted from the septic process (patient died, spleen was greatly enlarged). In Case 6 the blood counts were too high (hydremia?). In Case 8 the blood counts were too low. This patient had an enlarged spleen, and possibly the dose of blood transfused had not rightly been committed, as there had been trouble in this transfusion.

In all other cases the difference was less than 25 per cent. In thirteen cases it was even less than 0.3 million.

It appears to me that the method may be of practical value for those who are employing blood transfusion as a therapeutic agent in cases of chronic anemia. In acute hemorrhages it is not necessary to make an estimation by this method, because the blood findings in these cases are without great value. Small differences always will be seen, as the normal blood count varies within fairly wide limits. Too low a count may be due to an abnormal condition of the bone marrow, or an enlarged spleen and liver, when the blood corpuscles are prevented from entering the circulation, or to a rapid destruction in these organs of the introduced blood.

Too high counts possibly may be caused by a watery condition of the blood of the recipient (hydremia) in combination with bad vasotonus, the normal tonus returning after transfusion, which gives concentration of the blood and relative rise of red corpuscles.

It is obvious that pernicious anemia will give capricious results, as all these conditions may be present.

In adults the method may serve as a guide. A person weighing about 70 kg. needs $70 \times 15 = 1$ liter of blood to make his red blood cells increase one million.

CONCLUSION

In cases of simple anemia, there exists a correlation between the amount of blood transfused, the body weight and the rise of red blood cells. A rise of one million corresponds with an amount of 15 c.c. of blood per kg. of body weight. This gives a method to estimate beforehand the amount of blood to be transfused, as shown in twenty cases from the Leiden pediatric clinic.

THE DIAGNOSIS AND TREATMENT OF INTRACRANIAL HEMORRHAGE IN THE NEW-BORN

A REPORT OF FOURTEEN TREATED CASES *

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A review of the literature published on this subject within the last ten years leaves us with the impression that considerable confusion still exists as to the etiology and diagnosis of this condition, while the treatment advocated appears to be of rather a hit or miss type for the most part. We are, therefore, suggesting an etiologic classification, together with methods of diagnosis and treatment which have so far proved adequate in our hands. This is based on a series of fourteen treated cases, five of which ended in death. Necropsies performed in three of these fatal cases demonstrated that in these particular cases any treatment would have been unavailing. One other patient died of definite hemorrhagic disease with symptoms of complicating hemorrhages in other organs, and the fifth patient died one month after an operation which gave complete relief of symptoms for two weeks.

It is now universally admitted that intracranial hemorrhage in the new-born is a very common condition, that the resultant mortality is high, and that the resultant morbidity is probably as high and certainly is of more importance. Hedren,[1] in an article abstracted by Frazier, found that intracranial hemorrhage occurred in 9.28 per cent. of 700 infant cadavers examined by him. Schuman [2] states that from 2 to 13 per cent. of all postmortems on the new-born show intracranial hemorrhage. Schott [3] places the mortality from this cause following asphyxia in the neighborhood of 30 per cent., and Deluca [4] found varying degrees of intracranial hemorrhage in 36 per cent. of 554 infant cadavers examined since 1907. Warwick,[5] in a recent paper which was the report of a

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* Received for publication, July 7, 1922.

* Read at the meeting of the Cambridge Medical Improvement Society, March 27, 1922.

* The majority of the cases outlined in this paper have been seen by either one or both of us at the Boston Lying-in Hospital.

1. Hedren, G.: Intracranial Hemorrhage in the Newly-Born, Svenska Läk.-Sällsk. Handl. **44**:53, 1918; abstr. in Progr. Med. **1**:51, 1919, and Am. J. Dis. Child. **18**:290 (Sept.) 1919.

2. Shuman, J. W.: Intracranial Hemorrhage in the Infant, with History and Necropsy and Report of a Case, J. A. M. A. **63**:170 (Nov. 14) 1914.

3. Schott: Mortality of the New-Born Arising in Labor, Arch. f. Gynäk. **2**:316, 1920; abstr. in Progr. Med. **3**:79, 1921.

4. Deluca, F. A.: Jaundice in the New-Born, Semana méd. **28**:45, 1921; abstr., J. A. M. A. **78**:766 (March 10) 1922.

5. Warwick, M.: Necropsy Findings in New-Born Infants, Am. J. Dis. Child. **21**:448 (May) 1921.

study of 200 necropsies on infants dead within the first week of life, gives the incidence of cerebral hemorrhage as from 43 to 50 per cent. Approximately two-fifths of these cases were definitely due to hemorrhagic disease. The figures given by Hedren and Schuman are probably low, and it is safe to say that in from 35 to 40 per cent. of all infants dying within the first seven days of life, the cause of death will be found to be an intracranial hemorrhage.

Morbidity statistics are more difficult to compile, but every pediatrician will bear witness to the frequency of Little's disease or cerebral spastic paralysis in their clinics, and it is probable that at least one third of all such cases may definitely be traced to a birth hemorrhage within the skull.

The diagnosis and treatment of intracranial hemorrhage in the new-born depends on two main factors: first, the etiology of the hemorrhage, and secondly, the recognition of the fact that the production of symptoms in these cases is chiefly due to the increase in intracranial pressure produced by the presence of the hemorrhage, and not to the hemorrhage itself.

Before considering this aspect of this condition, we wish to emphasize certain anatomic and physiologic peculiarities of the new-born which we believe are not appreciated as they should be.

CEREBRAL ANATOMY OF THE NEW-BORN

Certain variations from the adult anatomy of the skull and brain are seen in new-born infants which are sufficiently important in their relations to the diagnosis and treatment of intracranial hemorrhage in these patients to warrant repetition and emphasis here. Brindeau[6] and others have referred to the important fact that the cerebral veins which join and empty their contents into the sinuses are many in number. Partly owing to their thin walls, but probably chiefly owing to the fact that their terminal segments are free and unsupported for a measurable distance after leaving the pia and before entering the sinus, these veins are extremely prone to rupture. They are most numerous and probably most important in the frontal and parietal regions. They are grouped in the immediate vicinity of all the sutures, particularly the frontoparietal and the sagittal.

The diplöe[7] does not appear until the second year. Browning[8] has shown that the pacchionian bodies are absent at birth and are a matter of postnatal development, probably not completed until the twentieth year, or thereabouts.

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[6] Brindeau, A.: On Trephining in the New-Born, Arch. mens. d'obst. et de gynec., Paris **10**:103, 1918.

[7] Piersol: Anatomy **1**:231, 1907.

[8] Browning, W.: The Anatomical Cause of the Frequency of Hydrocephalus in Childhood, Med. Rec. **89**:959, 1916.

The middle meningeal artery usually runs straight up the squamosphenoidal suture instead of backward, and divides into three branches rather than two only. The rolandic area lies adjacent to and immediately posterior to the coronal suture and runs parallel with it. The fontanels, contrary to what appears to be the common opinion, are covered with two main layers only; the skin and superficial fascia, and the membranous interosseous layer of tissue which consists of fused periosteum and dura, it being impossible to separate the two.

THE CEREBROSPINAL FLUID IN THE NEW-BORN

Frazier,[9] in 1915, reviewed what was known at that time in regard to the physiology of the cerebrospinal fluid. Since then Dandy [10] and others, working with experimental animals and hydrocephalic children, have confirmed the previous work, so that now our knowledge of the secretion, location, absorption and pressure of the cerebrospinal fluid rests on a firm foundation. The cerebrospinal fluid is secreted in the four ventricles by the choroid plexus, is distributed throughout the entire subarachnoid space, both spinal and cerebral, and is absorbed therefrom into the cerebral venous sinuses at a pressure normally equal to that within the sinuses. In adults the absorption takes place, in part, at least, by way of the pacchionian bodies. As has been pointed out in the previous section, the pacchionian bodies are absent at birth and it is, therefore, fair to assume that the possible avenues of escape for the cerebrospinal fluid from the subarachnoid space into the cerebral venous circulation are considerably diminished. This absorption in adults takes place at a normal pressure of from 8 to 10 mm. mercury which is equal to the pressure in the cerebral venous circulation. In new-born infants this pressure is somewhat lower, probably between 5 and 8 mm. mercury, although it has been placed as low as from 2 to 5 mm. by Sidbury.[11] Certainly, a cerebrospinal fluid pressure of 10 mm. mercury or over in the new-born is not normal. This pressure varies directly with and is dependent on the cerebral venous pressure. A rise in venous pressure will cause an immediate and compensatory rise in cerebrospinal fluid pressure due to a decrease in the amount of cerebrospinal fluid absorbed into the venous circulation. This results in an actual increase of fluid within the subarachnoid space and ventricles. This increased intracranial pressure has been shown by one of us [12] to be the basic factor in the production of symptoms following injury to the brain in adults. A similar train of events occurs in the new-born.

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[9] Frazier, C. H.: The Cerebrospinal Fluid and Its Relation to Intracranial Lesions, Progr. Med. **1**:2, 1915.

[10] Dandy, W. E.: Experimental Hydrocephalus, Ann. Surg. **70**:129, 1919.

[11] Sidbury, J. B.: The Importance of Lumbar Puncture in Intracranial Hemorrhage of the New-Born. Report of Case, with Recovery, Arch. Pediat. **37**:545, 1920.

[12] Munro, D.: Indications for Operation in the Treatment of Injuries Involving the Brain, Boston M. & S. J. **186**:342 (March 11) 1922.

REFLEXES IN THE NEW-BORN

Changes in the reflex activity in the new-born, as exemplified by the changes in the classical deep reflexes, are frequently mentioned in the literature as diagnostic aides in cerebral evaluation of localization. It has been our experience that very little of value, other than as confirmatory evidence, can be obtained by noting the presence or absence of the classical deep reflexes in these new-born infants. Burr,[13] who worked with sixty-nine normal infants varying in age from 1 hour or less to 90 days—forty-two of them being 7 days or less in age—offers us abundant support for our observation. He found that the deep and superficial reflexes may be present at birth but that their absence does not indicate disease. Among these reflexes he included the following: knee, achilles, chin, plantar and abdominal. Of these the plantar was the most variable.

ETIOLOGY OF INTRACRANIAL HEMORRHAGE

These anatomic and physiologic peculiarities of the new-born, we believe, bear an important relation to the condition under discussion. A proper appreciation of them does much to explain the etiology and even more to clear up diagnostic difficulties, thus allowing us to formulate a reasonable method of treatment for this type of case.

Various etiologic classifications have been proposed in the past ten years for this disease. Up to Warwick's [14] proposed classification, which, by the way, appears to have escaped the notice of most authors who wrote on this subject following the publication of her paper, the favorite choice was a classification dependent on the location of the hemorrhage. That is, the cases were classified as either pretentorial or subtentorial. This was recognized to be not entirely satisfactory, since very many of these cases coming to necropsy showed hemorrhage in both localities. This classification also ignored the cases which show at the postmortem multiple petechial intracortical hemorrhages, and hemorrhages about the basal ganglia and in the pons and medulla.[15] Warwick, apparently, also considered the classification according to location unsatisfactory, chiefly, however, because by this method hemorrhagic disease as a cause of intracranial hemorrhage was not recognized. Green and Swift,[16] Schloss and Comiskey,[17] Soresi,[18] and Schloss,[19] all mention the possibility of a cause and effect relation between these two but lay no stress on it. Warwick for the first time proposed that intracranial hemorrhage be divided into three groups in such a way as to include this important condition as follows: (1) traumatic from moulding of the head; (2) cases of hemorrhage due to congestion or stasis with rupture of veins, and (3) cases of hemorrhage due to a diseased condition of the fetus, including in this group hemorrhagic disease and prematurity.

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[13] Burr, C. W.: Reflexes in Early Infancy, Am. J. Dis. Child. **21**:529 (June) 1921.

[14] Warwick, M.: Cerebral Hemorrhage of the New-Born, Am. J. M. Sc. **158**:95, 1919.

[15] Schwartz, P.: Birth Hemorrhages in Newly-Born, Ztschr. f. Kinderh. **29**:102 (April) 1921.

We believe this to be an essentially correct method of grouping these cases from an etiologic point of view, but feel that asphyxia as a cause for congestion and stasis with rupture of cerebral veins is sufficiently important to demand consideration. There is, to be sure, little, if any, direct evidence that an abnormal increase in the carbon dioxid content of the blood will cause venous congestion, and as far as we know no evidence to show that clinically asphyxiated babies show this blood picture at birth. It is, therefore, incorrect to speak of any new-born baby as being asphyxiated from the strictly scientific point of view. Nevertheless, obstetricians recognize a clinical type of asphyxia which exists at, or before, birth to a varying degree. During labor a sudden change in fetal heart rate which is constant, the cessation of pulsation in the umbilical cord, and the coming away of meconium are considered sufficient evidence to justify the diagnosis of fetal asphyxia and call for more or less radical measures up to immediate delivery for the correction of the condition. At birth, clinically asphyxiated babies are cyanotic, do not start breathing well, or cry, and require treatment which is directed toward the artificial stimulation of respiration. Once respiration is started, the color returns to normal, the baby regains its muscular tone, and in the majority of cases remains a normal baby. It has also been repeatedly observed that these clinically asphyxiated babies, when they die, die from respiratory failure, the heart continuing to beat for some time after the respiratory center has definitely ceased to function, and after it will no longer react to artificial stimulation. Until this clinical evidence can be disproved by chemical studies of the blood of the new-born infant, therefore, we must consider the baby exhibiting the above symptoms as asphyxiated.

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[16] Green, R. M., and Swift, J. B., Jr.: Hemorrhagic Disease of the New-Born, Boston M. & S. J. **164**:454, 1911.

[17] Schloss, O. M., and Commiskey, J. J.: Spontaneous Hemorrhage in the New-Born, with a Report of Nine Cases, Am. J. Dis. Child. **1**:276 (April) 1911.

[18] Soresi, A. L.: Hemorrhagic Conditions in Children; Pathology; Etiology; Treatment, Arch. Pediat. **30**:225, 1913.

[19] Schloss, O. M.: Etiology of Hemorrhage in the New-Born, Arch. Pediat. **30**:276, 1913.

Is this clinical asphyxia related to congestion and stasis in the cerebral veins? Evidence sufficient to warrant a definite answer to this question is also lacking. There are, however, certain suggestive clinical observations. A condition of peripheral venous congestion is present in all of these babies as borne out by the cyanosis. Pressure from one cause or another on the umbilical cord, sufficient to interrupt either partially or completely the circulation therein, has long been recognized by obstetricians as a definite cause for fetal asphyxia accompanied by the symptoms enumerated above.

Necropsies performed on babies dead of asphyxia show petechial hemorrhages and congestion of abdominal and thoracic organs.[20] This picture has been thought to be due to hemorrhagic disease but no evidence to support this view has been advanced, and in the face of analogous pathologic findings in adults dead of suffocation, this latter hypothesis is open to question. Doazan,[21] in 1913, pointed out the relationship between asphyxia and intracranial hemorrhage and Manton [22] mentions the findings of punctate subcortical hemorrhages at a necropsy on a patient dead of suffocative asphyxia and quotes some figures to show that children asphyxiated at birth show a higher percentage of abnormal nervous development in later life. Bailey [23] also mentions it as a cause of hemorrhage, as does Strachauer [24] but it remained for Schwartz [15] to put it on a definite basis, as the result of careful microscopic examination of the brains of thirty infants with histories of asphyxia. These showed, in the early cases, punctate hemorrhages all through the brain, and in later cases softening in localized areas. Schott [3] also publishes some interesting statistics on the morbidity relations of asphyxia and idiocy, epilepsy and the like.

As shown above, these asphyxiated babies die of respiratory paralysis. A further analysis of this picture reveals a close similarity to the condition seen in persons dying from what is recognized as medullary edema. This is most commonly seen as the terminal stage of the sequence of events brought on by a severe injury to the brain in adults. The primary stage in this adult condition is congestion and stasis of the cerebral venous circulation.[12] Cerebral venous pressure and cerebrospinal pressure increase synchronously, a rise in the first causing an immediate and relatively equal rise in the second.[25, 12] Excessive cerebrospinal hypertension causes death from respiratory paralysis due to medullary edema.

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[20] Ehrenfest, H.: Birth Injuries of the Child, D. Appleton & Co., 1922.

[21] Doazan, J.: Etiologie, symptòms et traitement chirurgical des hémorragie méningées du nouveau-né, Arch. gén. de chir., Par. **9**:10, 1913.

[22] Manton, W. P.: Asphyxia Neonatorum and Its Sequelae, New York State J. M. **14**:302, 1914.

[23] Bailey, H.: Cranial and Intracranial Birth Injuries, Am. J. Obst. & Gynec. **1**:52 (Oct.) 1920.

[24] Strachauer, A. C.: The Surgical Treatment of Cerebral Hemorrhage in the New-Born, Minnesota Med. **3**:577, 1920.

[25] Keen's Surgery **3**:190 et seq. Philadelphia, W. B. Saunders Company.

It has been our impression that by far the greater number of subjects showing symptoms—not necessarily fatal—from intracranial hemorrhage can be demonstrated to have been suffering from a definite degree of either intra-uterine or intrapartum asphyxia.

In view of this indirect evidence and because clinical asphyxia has come to be a condition commonly diagnosed both in the fetus during labor and in the new-born infant immediately after delivery, we feel that asphyxia should be given at least a temporary recognition as an etiologic factor in the production of intracranial hemorrhage in the new-born and propose, therefore, to modify Warwick's classification in such a way as to include such cases in a separate division. Since we have done this, we have found that the number of cases of intracranial hemorrhage which might properly be classed as traumatic in origin is relatively quite small. Nevertheless, as long as fracture of the skull occurs, and as long as there continues to be a tearing of the sinuses and meninges by excessive overlapping of the sutures, so long will it be necessary to classify certain of these cases as strictly traumatic in origin. Our classification is as follows:

1. Traumatic group—hemorrhage caused by excessive molding of the head and overriding of the sutures.
2. "Asphyxia" group—hemorrhage caused by excessive cerebral venous congestion with rise of intracranial pressure.
3. Fetal disease group—the hemorrhage in these cases having no relation to the labor, but being most commonly caused by hemorrhagic disease and rarely by syphilis or other toxemias.

DIAGNOSIS

In the diagnosis of intracranial hemorrhage in the new-born, we have come to rely on three main criteria. These are the history and physical examination, the measurement of the intracranial pressure by spinal manometer, and the determination of the coagulation and bleeding time. By the proper evaluation of findings under these three headings we feel that we are able to sort out our cases according to the etiological classification just proposed, and are thereby prepared to suit our treatment to the case rather than, as has been done in the past, endeavor to suit the case to a given method of treatment.

Hemorrhagic Disease Cases.—The simplest cases to classify for treatment are those of hemorrhagic disease of the new-born, in which the intracranial hemorrhage is merely a symptom of a more extensive pathologic condition. A great deal of work has been done on the diagnosis and treatment of this condition in recent years, and while even now the causation and pathology are not clearly understood, we can, nevertheless, diagnose it with fair accuracy and treat it efficiently. The diagnosis, at present, rests on the determination of an increase in the bleeding and coagulation times of the blood of the infant. Rodda[26] not only determined the normal times, but also devised a method for carrying out this procedure that is simple, quick and sufficiently accurate. It is not necessary to go into the details of this method, except to say that it depends on the observation of the length of time a wound of given depth will bleed, and also on the length of time it takes a drop of blood to clot sufficiently to hold a small lead shot from moving within it. The normal bleeding time for the new-born is from two to five minutes, and the normal coagulation time from five to nine minutes. Cases of intracranial hemorrhage showing a prolonged bleeding and coagulation time should be classed and treated as hemorrhagic disease cases regardless of other physical findings or of the history. Intracranial hemorrhage due to syphilis or other toxemias may occur, but is very rare. Hedren[1] in a study of 700 infant cadavers found only three to be syphilitic, while intracranial hemorrhage was present in more than 9 per cent.

Traumatic Cases.—The diagnosis of traumatic intracranial hemorrhage should be made only in cases with a definite history of trauma. Many cases, but unfortunately not all, will show evidence of trauma on examination. Depressed and comminuted fractures of the skull, with or without laceration of the brain, present no great difficulty in diagnosis. Laceration of the meninges, tearing of the sinuses, or the cerebral veins entering the sinuses, on the other hand, present a more difficult problem. Here the history is of value. A large head, a small pelvis, a precipitate or long protracted labor, or other obstetric complication requiring excessive molding of the cranial bones, are of importance as evidence. If combined with this history there is manometric evidence of a marked increase in cerebrospinal fluid pressure and possibly blood in the cerebrospinal fluid in large amounts, the diagnosis can be made with probability. We do not believe that subdural puncture as suggested by Green,[27] Simmons,[28] Gilles,[29] and Doazan,[21] is either an accurate or a justifiable procedure in this or any other type of intracranial hemorrhage. It is difficult for us to conceive of a strictly subdural hemorrhage so large in amount as to be recognized by this method, which would not be subarachnoid, in part at least, and we believe that the chances of making a subdural rather than a subarachnoid puncture by the method described are very small. It is also unjustifiable because any subarachnoid hemorrhage will show in the cerebrospinal fluid at lumbar puncture, and, in addition, if at the same time, a manometric measurement of the cerebrospinal fluid pressure is made during this lumbar puncture, an accurate picture of the amount of intracranial hypertension is obtained; an important piece of information which cannot be obtained easily in any other way. Visual inspection of the fontanel following incision of the scalp, as recommended by Towne and Faber,[29a] who quote Murphy's original article in which this procedure was first recommended, does not appeal to us either, although it has not the objections that apply to subdural puncture. At best, only a very limited area is open to inspection, and information obtained by this method is available by lumbar puncture in addition to other more valuable evidence.

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[26] Rodda, F. C.: Studies with a New Method for Determining the Coagulation Time of Blood in the New-Born, Am. J. Dis. Child. **19**:269 (March) 1920. Ibid.: The Coagulation Time of Blood in the New-Born; with Especial Reference to Cerebral Hemorrhage, J. A. M. A. **75**:452 (Aug. 14) 1920.

[27] Green, R. M.: Intracranial Hemorrhage in the New-Born, Boston M. & S. J. **170**:682, 1913. Ibid.: Further Experience in the Treatment of Intracranial Hemorrhage in the New-Born, ibid. **174**:947, 1916.

[28] Simmons, C. C.: Two Cases of Intracranial Hemorrhage in the Newly-Born Relieved by Operation, Boston M. & S. J. **166**:43 (Jan. 11) 1912.

[29] Gilles, R.: Deux observations d'hemorragie méningée chez le nouveau-né; guérison aprés ponction décompressive par voie lombaire dans un cas, par voie crânienne dans l'autre; état ulterior des petits malades et considérations théraputique, Rev. mens. de gynéc., d'obstét. et de pédiat. **7**:465 (July) 1912.

"Asphyxia" Cases.—Cases of intracranial hemorrhage due to so-called asphyxia occurring either during labor or during delivery, will, we believe, come to be recognized as the largest class of intracranial hemorrhage cases in the new-born. In reviewing the literature for the past ten years, it is striking how few cases are reported in which there were any but massive hemorrhages within the skull. This was noticeable not only in those case reports which had to do with the treatment of the condition, but also in the necropsy reports. In view of our observations, we cannot but believe that many cases of intracranial hemorrhage in the new-born causing nonfatal symptoms have previously been allowed to progress for the most part undiagnosed and untreated. Schott [3] published some extremely interesting figures in regard to the morbidity following asphyxia at birth. Two and four-tenths per cent. of cases showing permanent central nervous system changes in later life gave a history of temporary asphyxia at birth. Asphyxia resulting from pressure on the cord, premature birth before twenty-eight weeks, and pressure on the infant's brain, raised the early mortality to around 30 per cent. This work is confirmed by Schwartz [15] who reports a series of necropsies on thirty infants all of whom suffered from asphyxia during labor or delivery.

The diagnosis in these cases depends on the finding of increased intracranial pressure by manometer, microscopic blood in the cerebro-

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29a. Towne, E. B., and Faber, H. K.: The Diagnosis and Treatment of Intracranial Hemorrhage of the New-Born. A Report of a Case, California State J. M. **20**:17 (Jan.) 1922.

spinal fluid, and a history of a prolonged or dry labor, deep anesthesia or prematurity. At the end of a few hours or days these babies nurse poorly or not at all, and have a peculiar shrill cry. These are the only symptoms that we have found to be at all constant. The classical symptoms of cyanosis, convulsions, spastic and flaccid paralysis, cranial nerve palsies, nystagmus, and bulging fontanels may all be either present or absent according to the individual peculiarities of the case.

"Asphyxia" may be either intra-uterine or intrapartum. It may be caused by a prolonged labor due to dystocia of any sort, pressure on the umbilical cord, rigidity of the mother's soft parts,[14] dry labor, prolongation of the interval between the birth of the head and the after coming shoulders, thus permitting two-thirds of the body to be subjected to intra-uterine pressure while one-third is subjected to atmospheric pressure,[15] contraction of the placental site with overlapping of the contracting uterine fibers and resulting diminution in the size of the placental sinuses and impaired oxygenation of the fetal blood,[30] and prolonged anesthesia of the mother, which are some of the causes not inherent in the fetus itself. Prematurity and congenital heart disease have been mentioned as causes belonging to this latter class.[14]

This "asphyxia," from whatever cause, raises the cerebral venous pressure and produces a venous congestion.[12] This rise in venous pressure decreases the amount of absorption of cerebrospinal fluid, and, as the secretion of this fluid is still going on in a closed space, causes a rise in intracranial pressure. This intracranial pressure rise produces more venous congestion in addition to an actual injury to the brain tissue,[31] thus establishing a vicious circle. At some point in this circle the venous congestion becomes sufficiently great to rupture one or more of the cerebral veins. This may occur in the meninges or in the substance of the brain itself, or in both locations. The primary cause of the rupture of the vein, and consequently of the hemorrhage, is the "asphyxia." The cause of the symptoms is the intracranial hypertension.[12] The symptoms may be exaggerated and made more severe by adding an intracranial hemorrhage to an acute hydrocephalus, but treatment of the hemorrhage alone will do nothing toward the relief of the hypertension, while, on the other hand, relief of the hypertension will probably prevent further hemorrhage and also promote proper absorption of whatever hemorrhage there may be that may have already taken place. This intracranial hypertension may be measured by the spinal manometer, and according to its degree lends itself to very definite methods of treatment.

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[30] Irving, F. C.: Cerebral Hemorrhage of the New-Born, Boston M. & S. J. **184**:539, 1921.

[31] Abt: Editorial Comment, Pract. Med. Ser. **4**:28, 1921.

SYMPTOMATOLOGY

Increase in Intracranial Pressure.—All victims of intracranial hemorrhage of the new-born are suffering from a complicating acute hydrocephalus, whether the hemorrhage is due to "asphyxia," to hemorrhagic disease or to trauma. Whatever the symptoms in these cases, they are made worse and carried to a fatal result only by virtue of the increase in intracranial pressure. Treatment directed toward removing a fresh hemorrhage from within the skull cavity will be successful only under the most favorable conditions; namely, a small clot on the surface of the brain or within the meninges, which can be localized previous to its removal, and which is so situated in relation to the skull that its removal is surgically possible. Only under these conditions can we possibly hope to treat successfully the hemorrhage itself. If, while doing this, we happen to make a sufficiently large opening to decompress the brain, then we may also, by chance, treat the underlying intracranial hypertension, which untreated, frequently causes the patient's death. If, on the other hand, we definitely attempt to treat the intracranial hypertension, we may prevent the death of the patient even though the hemorrhage itself be untreated. With the patient alive there is a chance that the clot will absorb and cause no symptoms in later life. Analysis by Frazier,[32] of Warwick's [14] reported series shows eight cases that might possibly have been surgical as against ten that were definitely nonsurgical from the operative point of view. Schwartz's [15] series of thirty cases were all such as to preclude any possibility of removing the hemorrhage. The cases of ventricular hemorrhage reported by Ballantyne [33] were all nonsurgical from the point of view of treating the bleeding, while 16 per cent. of the cases of intracranial hemorrhage studied by Hedren [1] were also definitely nonsurgical. Frazier [34] states that in the vast majority of these cases the hemorrhage is bilateral and consequently not subject to operative intervention. From the other point of view, the cases in which an attempt has been made to drain or remove the hemorrhage have been successful only in part, and even those cases reported as cured following operation can only be considered as temporarily cured until the children have grown old enough to demonstrate that they are normal mentally; a matter of at least five years, and a condition which has not been fulfilled in any of the "cured" cases. Drainage of the clots as performed by Simmons,[28] Green,[27] Gilles,[29] Cumston,[35] and others without question only removed a portion of the hemorrhage, and it is fair to say that in those cases in which the coronal suture was incised, the decompressive effect probably had quite as much influence as the actual removal of the blood itself. Removal of the clot through an osteoplastic flap is followed, in spite of the accompanying decompression, by a practically prohibitive operative mortality. To date this has been performed eighteen times with eight operative recoveries and as yet it is still too soon to be able to tell whether or not there has been any permanent injury to the central nervous system in these latter cases. On the other hand, lumbar puncture has been practiced by Doazan,[21] Lippman,[36] Brady,[37] Sidbury,[11] Foote,[38] Conti,[39] Vaglio,[40] DeStefano,[41] Gilles,[29] Green,[27] and Strachauer[24] with certainly a degree of success which is equal to that attained by other methods, and not, as might be supposed, limited to hemorrhages situated below the tentorium. Although Sidbury,[11] Strachauer,[24] and DeStefano[41] were the only ones to emphasize the importance of this procedure from the point of view of intracranial pressure, and Sidbury[11] was the only one who published his measurements of this pressure, nevertheless, the result accomplished was the same in all cases. It must, therefore, be evident that from every point of view the important diagnostic point in all these intracranial hemorrhage cases is the determination of the presence and the degree of increase in the intracranial pressure, and the localization of the hemorrhage sinks to a place of secondary importance beside this important evidence.

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[32] 32. Frazier, C. H.: Progr. Med. **1**:20, 1920.

[33] 33. Ballantyne, J. W.: Cerebral Ventricular Hemorrhages at and Soon After Birth, Edinburgh M. J. **25**:63 (July) 1920.

[34] 34. Frazier, C. H.: Surgical Aspects of Birth Traumata, Virginia M. Semi-Month. **18**:426, 1913.

[35] 35. Cumston, C. G.: Meningeal Hemorrhage in the Newly-Born Infant, Internat. Clin. **2**:226, 1914.

Supratentorial and Infratentorial Hemorrhage.—Typical cases of either supratentorial or infratentorial hemorrhage will show signs and symptoms peculiar to their respective locations. These occur, however, only in characteristic cases in which the hemorrhage is located in the meninges and strictly limited by the tentorium. The infratentorial cases which fall within these limitations run a course that is comparable to that which is recognized in adults as being due to compression and edema of the medulla of a very acute type. The patients are listless, cyanotic and may show convulsive respiratory seizures with

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36. Lippman, M. J.: Meningeal Hemorrhage of the New-Born, Complete Recovery; Report of Case, New York M. J. **103**:263 (Feb. 5) 1916.

37. Brady, J. M.: Lumbar Puncture in Meningeal Hemorrhage of the New-Born, J. A. M. A. **71**:347 (Aug. 3) 1918.

38. Foote, J. A.: The Hemorrhagic Tendency as a Frequent Cause of Cranial Hemorrhage of the New-Born, Am. J. Dis. Child. **20**:18 (July) 1920.

39. Conti, L.: Cerebral Hemorrhage in an Infant, Pediatria, Naples **29**:4, 1921; abstr. J. A. M. A. **76**:1137 (April 16) 1921.

40. Vaglio, R.: Intracranial Hemorrhage in the New-Born, Pediatria, Naples **29**:1, 1921; abstr., J. A. M. A. **76**:688 (March 5) 1921.

41. DeStefano: Lumbar Puncture for the New-Born, Pediatria, Naples **30**:1 (Jan. 1) 1922; abstr., J. A. M. A. **78**:765 (March 10) 1922.

rhythmic or Cheyne-Stokes breathing. The pulse is at first slow and bounding and later becomes very rapid and feeble. There may be cranial nerve paralyses, but there is not usually a somatic motor nerve involvement, nor any bulging of the fontanel. These symptoms are due not to the hemorrhage, but rather to the pressure exerted on the medulla and pons by the presence of the hemorrhage in this particular locality combined with an acute intracranial hypertension.

Typical supratentorial cases in which the hemorrhage is located entirely above the tentorium pass through two stages if allowed to progress without treatment. In the first stage the children are restless, crying and fussing a great deal with usually a spastic paresis or paralysis. This condition is followed by spastic convulsions, either generalized or local, which are usually ushered in with a shrill cry. There may be cranial nerve palsies, most frequently seen as a paralysis of the facial, the abducens, or the hypoglossal. The fontanel is often tense or, at least, bulging. These symptoms are due to an edema and compression of the cerebral hemispheres, which are the result of the increase in the intracranial pressure and only secondarily due to the presence of the hemorrhage itself. If untreated, this condition progresses to compression and edema of the medulla, and the picture changes to that seen in typical infratentorial hemorrhages. Lumbar puncture in both these conditions shows an increase in intracranial pressure. Cerebrospinal fluid removed by lumbar puncture in the basal cases shows a concentrated mixture of blood with the fluid. In the supratentorial cases, this same condition may be present but usually the fluid will show only a tinge of color.

Reflexes and Localizing Signs.—In general, it may be said that the functional possibilities of the central nervous system depend on the medullation of the axone tracts.[42]

Those axones which enable the spinal cord to act as an organ per se acquire their medullary sheaths earlier than those having connections with the brain. In other words, the simpler reflex actions are acquired before the more complicated suprasegmental combinations. At birth all of the spinal cord fasciculi are medullated except the spino-olivary and corticospinal or pyramidal tracts.[42] These latter tracts become medullated sometime between the ninth month of intra-uterine life and the end of the second year. Normal voluntary muscular control is, therefore, acquired after birth. The most useful localizing signs in the lesions of the brain, other than those requiring the introduction of the higher associational centers, are demonstrable as alterations in the reflex arcs; as, for example, the increase or the loss of a tendon reflex, or

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42. Morris: Human Anatomy, 1914, Pt. 3, p. 791.

as alterations in voluntary muscular control, demonstrable as more or less limited spastic or flaccid muscular paralysis. It has been shown[13] that the normal reflex activity of the new-born, up to seven days, is so variable that alterations in it cannot be considered pathologic, and this, therefore, can be of no constant value in the localization of lesions in the brain. Medullation of the pyramidal tract may not be completed until the end of the second year of life. Normal voluntary motion of the skeletal muscles in the new-born is, therefore, at a minimum. Abnormal voluntary motions, or an abnormal lack of voluntary motion, due to a circumscribed cerebral lesion, such, for example, as a clot over one rolandic area, which in the adult would produce a monoplegia or hemiplegia, in the new-born might produce no demonstrable change in the pyramidal tract control, and could not, therefore, be localized A larger clot on the brain of the new-born, covering the entire cortex of one hemisphere, for example, even in the absence of an accompanying intracranial hypertension—an impossible condition, of course—by virtue of its extent and consequent massive irritation might create a sufficient amount of stimulus to irritate even a nonmedullated pyramidal tract. This in the new-born would show as a hemiplegia, while in the adult it would produce a much more complicated picture. In the former case, one would be tempted to localize the irritation about the cortical motor area, while in the latter case it would be apparent that the lesion could not be circumscribed to that extent. Motor paralyses and reflex changes in the new-born, therefore, are of doubtful value from the point of view of cerebral localization, and dependence on these signs may lead one into diagnostic errors which may result in mistaken or incomplete methods of treatment. Sensory changes of central origin and certain cranial nerve palsies require cooperation of the patient for their detection, a condition which cannot be fulfilled in these patients. Other cranial nerve involvement, such, for example, as shown by paralysis of the facial, the oculomotor, and the hypoglossal supply can be demonstrated successfully in the newborn, but such paralyses are of very little value from the diagnostic point of view, unless other evidence is present which will help to place the causative factor above or below the tentorium. Other signs, such as changes in the eyegrounds, alterations in blood pressure, and alterations in the respiratory and pulse rates, are either inconstant, or so difficult to obtain as to make them of little practical value, and, in any event, these changes are due not to the hemorrhage but rather to the underlying increased intracranial pressure which can be more accurately demonstrated in other ways.

Lumbar Puncture in the New-born.—Lumbar puncture in the new-born would appear to be an extremely simple matter. It has been our experience, however, that it presents technical difficulties which make it a much more troublesome procedure than in the adult. From the point of view of a successful puncture, the most important person involved in the procedure, other than the patient, is the one who holds the baby. It is impractical and unnecessary to use local or other forms of anesthesia in these cases, and this person, therefore, must be comfortably and firmly placed so that the movements of the baby during the operation can be controlled properly. The baby should be placed on its left side with the spine arched. This is accomplished by drawing the head and the knees together as far as possible without causing interference with the respiration. The spine should be horizontal, and the vertebral spines parallel with the table. In our experience the puncture may safely be made in either the third or fourth lumbar space. Punctures at a lower level than the fourth lumbar space are very much more difficult. Bleeding from the trauma of the needle we have found to be very common unless particular pains are taken with the technique. We believe this to be due to injury to the spinal veins. These are divided into two plexuses lying more or less in the midline, one on the outer aspect of the posterior portion of the dura in a line with the vertebral spines, and the other on the anterior aspect of the anterior layer of the dura between it and the posterior aspect of the vertebral bodies.[43] Puncture made in the line of the vertebral spines frequently results in hemorrhage from the posterior plexuses while insertion of the needle to so great a depth as to traverse the entire subarachnoid space from behind forward with resultant wounding of the anterior layer of dura also causes hemorrhage due to laceration of the veins of the anterior plexus. We have, therefore, adopted the method of inserting the needle from one side of the median line in a medialward and upward direction, and take great pains to make sure that it shall not be inserted to too great a depth. The size of the needle, within limits, makes very little difference. We use with satisfaction as large a size as fourteen gauge. Care should be taken to see that the needle is short pointed with sharp edges and point, as otherwise it is difficult to pierce the flimsy arachnoid of these new-born infants. Spinal manometric readings normally are below 10 mm. mercury and probably average around 6 mm. Respiratory fluctuations of pressure are visible in the manometer.

TREATMENT

Treatment of intracranial hemorrhage in the new-born depends primarily on the successful etiologic classification of the individual case, and secondarily, on the recognition and treatment of the increased intracranial pressure that is present in every case.

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[43] Frazier, C. H.: Surgery of the Spine and Spinal Cord, 1920, p. 23; Piersol's Anatomy, 1907, p. 897.

Intracranial Hemorrhage of Hemorrhagic Disease Origin.—Intracranial hemorrhage cases in which the bleeding is but a symptom of a general hemorrhagic diathesis, can be and should be recognized by an increase in the bleeding and coagulation times of the blood. Any case of intracranial hemorrhage in a new-born infant may fall into this class regardless of the presence or absence of other confirmatory symptoms. It is, therefore, necessary to determine the bleeding and coagulation times in every intracranial hemorrhage case in order that this type of case may receive appropriate treatment. This treatment in its broadest aspects requires the administration of normal blood either subcutaneously or intravenously. Both methods have been strongly recommended and have entirely replaced the older methods of administering rabbit serum, hemostatics, and the like.[16] Ashby [44] recommends both methods, Soresi [15] and Lespinasse [45] believe that transfusion should be practiced, while Schloss and Comiskey,[17] Foote,[38] and Rodda [26] prefer the subcutaneous method. We prefer the subcutaneous method not because it is necessarily any more efficient, but because we have found that the only practical place to transfuse a new-born infant is into the superior longitudinal sinus, and we have felt that the further addition of blood to the already congested cerebral venous system was particularly undesirable in this class of hemorrhagic case. Having administered whole blood subcutaneously in sufficient quantities to bring the bleeding and coagulation times back to normal, and presumably to have stopped the hemorrhage, we then proceed to reduce the intracranial pressure. This may be done by lumbar puncture and drainage of the cerebrospinal fluid if the manometric reading is 18 mm. mercury or below. If above that point, the intracranial pressure must first be reduced by either a ventricular puncture or a subtemporal decompression. We are as yet not prepared to say which of these two methods of cranial decompression is preferable in this type of case. In our series of fourteen cases, three fell within this group. Two of these patients died, one forty-two hours and the other sixty-five hours after delivery.

Case 1.—Baby E. had a large cephalhematoma and was bleeding from the anus. The cerebrospinal fluid pressure was 18 mm. mercury and was reduced to 7 mm. mercury by the withdrawal of approximately 7 c.c. of fluid which was almost pure blood. Previous to this 30 c.c. of mother's blood had been administered subcutaneously. Symptoms began thirty-six hours after birth, and were chiefly generalized convulsions with moaning and no cyanosis. Examination showed a large cephalhematoma, bleeding from the anus, opisthotonos, stiff neck, slightly tense but not bulging anterior fontanel, with a bilateral Babinski and ankle clonus. No cranial nerve involvement. As the symptoms continued unchecked following the lumbar puncture 30 c.c. of maternal blood was again given subcutaneously, but the baby grew steadily worse and died shortly after this. There was no necropsy.

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[44] Ashby, I. E.: Hemorrhagic Conditions in the New-Born, Med. J. Australia **1**:50 (Jan. 8) 1921.

[45] Lespinasse, V. D.: Hemorrhagic Disease of the New-Born. Treatment by Direct Transfusion of Blood, with a Clinical Report of Fourteen Cases, J. A. M. A. **62**:1866 (June 13) 1914.

Case 2.—Baby di V. first showed symptoms about ten hours after delivery. There were generalized convulsive seizures preceded by a shrill cry, during which the baby became cyanotic, stopped breathing and frothed at the mouth. Physical examination, including the neurologic examination, was essentially normal, except for the anterior fontanel which was tense and bulging. There was no external bleeding, but there was marked brawny subcutaneous edema in both loins and buttocks. Cerebrospinal fluid pressure was 20 mm. mercury but in spite of this 7 c.c. of cerebrospinal fluid was withdrawn, reducing the pressure to 8 mm. The fluid was almost pure blood and did not clot. Following the reduction of pressure the fontanel was noted as being depressed and soft, and the previous respiratory embarrassment was relieved.

Arrangements were then completed for the transfer of the baby to the Boston Lying-in Hospital. On arrival there the bleeding time was found to be nine minutes. The coagulation time was not done. Twenty cubic centimeters of paternal blood was given subcutaneously and 60 c.c. of salt solution was given intraperitoneally. Some hours later, the baby vomited coffee ground material and passed tarry stools. The fontanel was still depressed and soft and the baby looked bluish white and very sick. It died, probably of hemorrhage, about sixty-five hours after the onset of the symptoms.

Necropsy showed a massive subperitoneal hemorrhage in the posterior pelvic region and a cerebral hemorrhage which filled the entire spinal and cerebral subarachnoid space.

Case 3.—Baby R., colored, began to bleed from the nose two days after birth. Following this he vomited and passed by rectum large amounts of changed and fresh blood. The bleeding time was ten minutes and the coagulation time eight minutes. Fifteen cubic centimeters of whole blood was given intramuscularly. Three days after birth a nystagmus toward the left and a spastic quadriplegia were noted. Six cubic centimeters of maternal blood was given intramuscularly and the baby improved somewhat. Five days after birth the baby developed a fairly definite spastic quadriplegia with absent knee jerks and a bilateral Babinski. The rest of the examination was normal, except that the anterior fontanel seemed to be somewhat tenser than normal. There were no convulsions or cyanosis, but there was some pallor of the mucous membranes.

Lumbar puncture demonstrated a cerebrospinal fluid pressure of 12 mm. mercury, which was lowered to 4 mm. by the withdrawal of about 3 c.c. of yellow cerebrospinal fluid which proved by microscope to have red blood corpuscles in it. Following this, the baby was apparently well and normal in every way for fourteen days. At the end of this time it began to show some more spasticity and nineteen days after the last lumbar puncture it showed a definite spastic quadriplegia with a tense and elevated anterior fontanel. Lumbar puncture at this time showed a cerebrospinal fluid pressure of 20 mm. mercury. This was reduced to 9 mm. by the withdrawal of 25 c.c. of clear, colorless cerebrospinal fluid. There was considerable improvement following this but the symptoms were not entirely cleared up, so another lumbar puncture was performed two days later. The cerebrospinal fluid pressure this time was 14 mm. mercury, and 10 c.c. of clear, colorless fluid was withdrawn, reducing the pressure to 5 mm. Since that time, one month ago, the baby has been practically normal in every way.

This baby probably suffered from a meningismus due to the irritation of the clot which became less and less as the clot absorbed. From this small series of cases it would seem that intracranial hemorrhage due to hemorrhagic disease in the new-born carried with it a very high mortality in spite of treatment.

Intracranial Hemorrhage of Traumatic Origin.—Under this classification we have had three cases, two with complicating fracture of the skull, and one with hemorrhage from a rupture of the superior longitudinal sinus. Two of these babies are dead. Treatment in these traumatic cases is far from satisfactory from any point of view. Massive hemorrhages, such, for example, as occur following the rupture of a large venous sinus, while they produce an acute hydrocephalus that is amenable to and can be treated and corrected, are practically impossible to control. If uncontrolled, the patient dies of hemorrhage. If nature succeeds in controlling the hemorrhage by raising the intracranial pressure sufficiently high to close off the sinus, this high pressure of itself will be fatal, and, if reduced to normal, the sinus will again begin to bleed. Such a case follows.

Case 4.—Baby G., a 7 pound baby, was delivered following the application of a fillet to one foot in a breech presentation; the length of the labor is not noted. Four days after delivery it was noticed that the baby was not doing well and had a peculiar cry. Five days after delivery the baby became very cyanotic at times, breathed and nursed poorly, was very drowsy and the fontanels bulged markedly.

Examination revealed only a left spastic hemiplegia with a left ankle clonus.

Lumbar puncture showed a pressure of 30 mm. mercury and a drop of cerebrospinal fluid removed for examination proved to be practically pure blood. A right subtemporal decompression was made, and the brain was found to be under great pressure and covered with old clot. While finishing the operation the baby's condition became very poor and artificial respiration and oxygen were required. The pulse during this dropped to 70. The baby left the table alive, but died three-quarters of an hour later from medullary edema.

Necropsy showed a massive subarachnoid hemorrhage which filled entirely the spinal and cerebral subarachnoid spaces, a rupture of the superior longitudinal sinus and edema of the medulla.

This case demonstrates very clearly the futility of attempting to localize intracranial hemorrhage in the new-born, and what is more important, the value of lumbar puncture and measurement of the intracranial pressure early in order that decompressive steps may be taken before medullary edema sets in.

Case 5.—Baby E. had a depressed "tin plate" fracture of the right frontal bone with a right sided facial paralysis, spastic quadriplegia with bilateral ankle clonus, and an intracranial pressure by lumbar puncture of 22 mm. mercury with old blood in the cerebrospinal fluid. At operation it proved to be impossible to raise the depression so it was removed and a right subtemporal decompression also performed. Two weeks after operation the baby was reported as being well in every way, except for a slight facial paralysis.

One month after operation, however, it was reported as dead following a train of symptoms that were very suggestive of a meningismus with secondary increased intracranial pressure, but which in any event was not recognized and was allowed to go untreated.

Case 6.—Baby S. This case followed a rapid high forceps delivery on a child with a fairly large head. For two days following delivery, the child became more and more spastic, and on the second day presented a spastic quadriplegia with a bilateral Babinski and ankle clonus and with a cerebrospinal fluid pressure of 14 mm. mercury. This pressure was reduced to normal, the cerebrospinal fluid withdrawn being clear and colorless. There was some slight improvement for twenty-four hours, but the following day saw the baby practically moribund. Lumbar puncture demonstrated a pressure of 30 mm. mercury. As a result of this observation, a left subtemporal decompression was performed. In the course of this operation a comminuted fracture of the left temporal bone was found with laceration of the dura and underlying brain probably involving the left motor area at least. After a stormy convalescence the baby was discharged one and one-half months later with a spastic quadriplegia and probably considerable mental impairment.

This etiologic group, like the preceding one, carries its own high mortality and morbidity. While the mortality can doubtless be lowered by an earlier recognition of the underlying intracranial hypertension and its more adequate treatment, the morbidity of such severely injured cases as the last must always remain high. We cannot on that account, however, allow these cases to go untreated, because we can never tell in advance which case will be prevented from becoming a spastic idiot and merely become a spastic hemiplegic with a normal mentality by virtue of properly timed and properly conceived treatment.

Intracranial Hemorrhage Following Asphyxia.—We have classified eight cases of our series under this heading. Of these patients one only has died, the rest having been discharged at the end of from four to twelve days relieved and apparently normal in every way. One of these later developed meningismus, but following a ventricular puncture with the removal of 90 c.c. of cerebrospinal fluid, supplemented by two subsequent lumbar punctures with removal of about 20 c.c. more, was entirely relieved and apparently well.

Case 7.—Baby B., the only patient in this series that died, was first seen ten days after delivery, which followed a labor of twelve hours, the first ten and one-half hours being included in the first stage. There was moderate asphyxia at birth. For three days previous to the time it was seen it had been suffering from increasingly severe attacks of respiratory convulsive seizures with apnea lasting up to two minutes, marked cyanosis and general bodily rigidity. The heart rate during these attacks dropped from 128 to 45 and the fontanel was not abnormal. These convulsions were occurring about once every half hour. Between times the baby was apparently normal in every way.

Physical examination, including the neurologic examination, was normal. Lumbar puncture showed a cerebrospinal fluid pressure of 12 mm. mercury. Ten cubic centimeters of fluid with microscopic blood cells in it, and tinged pinkish yellow, was withdrawn and the pressure lowered to 4 mm. Two hours later another lumbar puncture was performed and the pressure, readings and amount of fluid withdrawn were identically as before. Following this, the needle tract remained open and cerebrospinal fluid drained until the baby's death, about twelve hours later. This occurred during a typical convulsion in which the pulse dropped to 68 and grew weaker, the respirations failed to start again and the baby died.

Necropsy showed marked congestion of all organs with microscopic petechial hemorrhages in the midbrain, pons and medulla. There was also edema of the medulla and endothelial cell infiltration of the basal meninges.

It is unfortunate that this case was allowed to go such a long time without treatment, although from the location of the hemorrhages at necropsy it is probable that the prognosis would have been fatal in any event.

The cases that ended in recovery can be grouped. All the infants showed at birth definite cyanosis and asphyxia which had presumably been caused during the labor. One baby was delivered by cesarean section, three by version, one by breech extraction, and two by normal deliveries. Dry labor was specifically noted as occurring three times. The symptoms varied. Four showed convulsions and only three associated cyanosis, five had definitely tense or bulging anterior fontanels, and in only two was there any cranial nerve involvement. Five showed some spastic paralysis, but only two showed pathologic reflexes. Sixteen lumbar punctures were done in the seven cases and in two ventricular punctures were also made. The highest pressure measured was 50 mm. mercury and the lowest 8 mm., each occurring only once. The average pressure was 17 mm. mercury. Fluid was withdrawn twelve times by lumbar puncture and in every withdrawal but one was either yellow or definitely tinged with blood not due to the trauma of the needle. One, the child that was delivered by cesarean section, showed marked jaundice with a rise in temperature. Infection, including meningitis, was definitely ruled out in this case before the diagnosis was made. The longest time elapsed in any one case before being discharged relieved to the pediatrician in charge was thirty-six days, and the shortest was four days. The average time under treatment was twelve days. All of these cases were discharged relieved with normal pulse, temperature and respiration, essentially normal physical examination, normal cry and ability to nurse, and all gaining weight.

From this series it can be seen that intracranial hemorrhage of "asphyxial" origin in the new-born, if treated from the point of view of acute hydrocephalus, carries with it a low mortality. This is especially evident on comparison with the mortality in the other two etiologic groups, notwithstanding the small number of cases involved.

Operative Treatment.—Our operative treatment has consisted of lumbar puncture, subtemporal decompression and ventricular puncture. Lumbar puncture has already been taken up and need not be again considered. Subtemporal decompression is indicated whenever the cerebrospinal fluid pressure rises above 18 mm. mercury in a traumatic case. Ventricular puncture is indicated whenever a posthemorrhagic meningismus has produced an intracranial pressure higher than 18 mm. mercury. Under other conditions we do not feel that we have as yet had sufficient experience to arrive at definite conclusions. We believe that eventually subtemporal decompression will be reserved for use only in those cases in which the intracranial pressure cannot be lowered permanently by a combination of lumbar and ventricular puncture

Ventricular puncture and subtemporal decompression in these infants should always be performed under local anesthesia. These children are already suffering from a compression of the medulla which involves the respiratory centers, and inhalation anesthetics are, in our opinion, extremely dangerous.

A typical subtemporal decompression should be performed if an opening is to be made into the skull through the bone. The reasons for this are the same as those that apply to subtemporal decompression in adults, namely, the opening is over a relatively silent area, the middle meningeal artery is exposed if desirable, and the decompression if properly made lies entirely beneath and protected by the temporal muscle.

The ventricular puncture should be made by way of the anterior fontanel, through the frontal lobe, and the needle caused to enter the anterior horn of the lateral ventricle. The point of election in the fontanel is at the most posterior portion of the junction of the mesial and posterior borders of the right frontal bone. The skin and membrane should be incised and the ventricle entered with a blunt needle. Every aseptic precaution should be observed and the operation should be performed in a hospital.

Hemorrhage from the scalp in these operations should not be controlled by any form of tourniquet. A tourniquet serves only to increase the already existing intracranial venous congestion. Such hemorrhage may be easily and promptly checked by the method evolved by Frazier, which consists of the application of spaced hemostats to the galea with eversion of the edges of the wound.

LATE RESULTS OF INTRACRANIAL HEMORRHAGE IN THE NEW-BORN

The late morbidity following intracranial hemorrhage in the newborn is quite as serious as the immediate mortality. Interesting statistical studies have been made on these cases of so-called Little's disease by Schott [3] and Sharpe.[46] The latter has demonstrated in 19 per cent. of the spastic children coming to his clinic an increase in intracranial pressure by spinal manometer. This is the only type of case considered by him to be a favorable subject for operative interference. Three hundred and fifty-eight subtemporal decompressions were performed. The operative mortality is given as 10 per cent. Most of the patients operated on obtained some relief, and many, especially those children under 3 years of age when operated on, have obtained practically complete relief.

In the course of the past year we have seen three cases of Little's disease. In all there was a history of difficult labor followed by various types and degrees of paralysis. One was mentally below par for its age, 2¼ years. There was a complete paralysis of several cranial nerves and the child was generally mildly spastic. Lumbar puncture was refused and the parents were advised to place the child in an institution. A second child, aged 3, had had an intracranial birth hemorrhage and a right parietal decompression at that time. He is now suffering from an increased intracranial pressure (30 mm. mercury) with a cerebral hernia through the ill judged decompression opening, and is under observation with a question of doing a decompression on the opposite side of the head. The third child is 6 years of age, with a left spastic hemiplegia and a definite history of injury at birth. His intracranial pressure is 11 mm. mercury and under orthopedic treatment his condition is improving markedly. Both these children are mentally normal.

Sharpe [46] makes no mention of the epileptics, but Frazier [34] summed up this situation in 1913. He limits the epileptics suitable for operation to those cases only which show a localizing motor sign. It has always been taken for granted in the past that the idiocy and epilepsy following untreated cerebral hemorrhage in the new-born is the result of the supra cortical blood clot. We do not feel that the evidence in favor of this is such that the accuracy of this statement can go unchallenged, especially in view of the recent work on intracranial pressure, and its relation to trauma, and the publication by Sharpe of the large series of cases cited above. These children are certainly worthy of any help that can be offered to them. At present they are a burden to their family, to the state institutions, and to themselves. They are passed from one pediatrician to another without ever getting any treatment other than platitudes. At orthopedic clinics they are equally unwelcome. The whole question of the pathology, diagnosis, and treatment of Little's disease should be reopened and an endeavor made to formulate an answer in the light of our more recent knowledge of

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46. Sharpe, William: The Diagnosis and Treatment of Brain Injuries, with and without a Fracture of the Skull, Philadelphia, J. B. Lippincott & Company, 1920, pp. 525, 650.

intracranial pressure. Even now much can be done as prophylaxis by the recognition of the hemorrhage as soon after birth as possible.[47]

CONCLUSIONS

1. We propose that the following etiologic classification of cases of intracranial hemorrhage in the new-born be adopted: (*a*) Traumatic group. (*b*) "Asphyxia" group. (*c*) Fetal disease group

2. The diagnosis of intracranial hemorrhage in the new-born should be based on the following: (*a*) The history and physical examination. (*b*) The measurement of intracranial pressure by spinal manometer. (*c*) The determination of the coagulation and bleeding times.

3. The treatment of intracranial hemorrhage in the new-born depends on (*a*) the successful etiologic classification of the case; (*b*) the recognition and measurement of the intracranial pressure.

4. The treatment of intracranial hemorrhage, due to hemorrhagic disease, consists of the administration of normal whole blood subcutaneously until the bleeding and coagulation times have returned to normal, and then appropriate relief of the intracranial hypertension.

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[47] The following references also bear on this subject:

Ballantyne, J. W.: The Nature and Management of Neonatal Diseases, Arch. Pediat. **38**:141 (March) 1921.

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5. The treatment of traumatic cases consists of the prompt elevation of depressed fractures, and the relief of the intracranial hypertension by drainage either by lumbar puncture or ventricular puncture as indicated, or typical subtemporal decompression.

6. The treatment of "asphyxia" cases consists of the relief of the intracranial hypertension by drainage either by lumbar puncture or ventricular puncture as indicated, or typical subtemporal decompression.

7. Cerebral localization of pathology in the new-born is rarely possible, and is, therefore, not amenable to surgical measures looking toward its correction.

8. The pathology, diagnosis and treatment of Little's disease should be studied more extensively from the point of view of intracranial pressure.

We wish to take this opportunity to thank the trustees, Dr. Newell, and the staff of that hospital for their kindness in allowing us to study and treat these cases.

CONGENITAL DEFICIENCY OF THE DIAPHRAGM *

JOHN STEPHENS LATTA

OMAHA

Recently there has been brought to the attention of the writer a case, encountered by Dr. C. W. Pollard in his practice, which presented the interesting and rather unusual condition of almost total deficiency of the left side of the diaphragm. Associated with and doubtless as a result of this, there were found some other minor anomalies, the most evident of which was a misplacement of some of the abdominal viscera into the left pleural cavity. It was obvious that these misplaced viscera represent a spurious hernia, due to an arrest in development of the left side of the diaphragm, rather than a true hernia due to a lack of diaphragmatic muscular tonus or development, for these viscera were not enclosed in a hernial sac but lay free in the left pleural cavity.

On reviewing the available literature concerning the subject of congenital diaphragmatic hernia it was found that the spurious type occurs most frequently. References have been found in this literature to 127 cases which could definitely be classified as spurious, due to defective diaphragmatic formation. The greater percentage of these deficiencies were found to occur on the left side, seventeen only being right-sided and the remaining 110 left-sided. No authenticated cases of complete lack of the diaphragm were found, although one such case was mentioned as having occurred (Bowditch [1]).

In the case of deficiencies on the right side, they were, in practically all cases, relatively small, admitting only a slight misplacement of abdominal viscera into the thorax, usually a small portion of the right lobe of the liver. In one case there was an extensive right-sided deficiency, which allowed the entire right lobe of the liver, all of the small intestine, the caecum and appendix, and the colon to pass into the right pleural cavity (Kocher [2]). Spencer [3] also described a similar case in which there was a large defect on the right side of the diaphragm, through which the right lobe of the liver, caecum and appendix, the small intestine, and the right kidney protruded into the right pleural cavity. St. Hiliare [4] gives an account of a case in which the right side of the diaphragm was lacking, admitting the stomach, small intestine, and the right lobe of the liver into the thorax. In seven of

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* From the Department of Anatomy, University of Nebraska, College of Medicine.

1. Bowditch, H. I.: Charleston M. J. **10**:396, 1855.
2. Kocher: Gerhardt's Handb. Kinderh. **6**: No. 2, 1880.
3. Spencer, H. R.: Tr. Obst. Soc. Lond. **32**:132, 1890.
4. St. Hiliare, G.: Schmidt's Jahrb. **121**:336, 1864.

the recorded cases of right-sided deficiency (Textor[5]) the size of the defect was not stated.

Cases with left-sided deficiencies, however, present considerable variation in the size of the defect, and, therefore equal variation in the amount of displacement of viscera. Of the 110 cases of this type, in sixty-eight there were large or medium-sized defects, in fourteen the defects were quite small, and in twenty-eight (Textor[5]) the size of the defect was not stated. In several cases it was stated that the entire left half of the diaphragm was wanting, and in a few others it was said to be represented only by a muscular band around the costal margin of the left side.

The small number of reported cases of right-sided hernias of the diaphragm are related, doubtless, to the position of the liver, as stated by Livingston.[6] It is doubtful, however, whether the presence of the liver on the right side influences the formation of the right pleuroperitoneal fold, or tends to eliminate the possibility of the occurrence of a deficiency. But it surely does decrease the possibility of misplacement of viscera into the right pleural cavity. As it is this misplacement of viscera which produces the pronounced symptoms in diaphragmatic hernia, it is very possible that there are many instances of right-sided diaphragmatic defect which produce no symptoms, and thus escape notice.

Only occasionally is the diaphragmatic defect accompanied by other developmental defects, except that of undeveloped lung, and in practically all cases the child is absolutely normal in external appearance. In one case (Abt[7]) the deficiency was accompanied by hypertrophy of the thyroid gland. In five instances (Gilford,[8] Giles,[9] Lacher,[10] Bischoff[11]) a considerable hypertrophy of the liver was noted. Seven cases were described of left-sided diaphragmatic defect associated with the development of accessory lungs (Cockayne and Gladstone,[12] Gruber,[13] Kohn,[14] Robsmann,[15] von Gossnitz,[16] Kaup[17]). Two cases were reported with an associated hemicephalous condition (Bischoff,[11] Grüber[18]), and one with hydrocephalous and also with intestinal occlusion (Grüber[18]).

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[5] Textor: Schmidt's Jahrb. **57**:64, 1864.
[6] Livingston, P.: Am. J. Obst., 1882, p. 733.
[7] Abt, I. A.: Arch. Pediat. **17**: 1900.
[8] Gilford, S.: Brit. J. Child. Dis. **1**: 1904.
[9] Giles, A. E.: Tr. Obst. Soc. Lond. **34**:132, 1892.
[10] Lacher, L.: Deutsch. Arch. f. klin. Med. **27**: 1880.
[11] Bischoff: Arch. f. Gynäk., 1885, p. 437.
[12] Cockayne, E. A., and Gladstone, R. J.: J. Anat. **52**:64, 1917.
[13] Gruber, G.: Beitr. f. path. Anat. u. allg. Path., 1914, p. 491.
[14] Kohn: Inaug. Diss. Königsberg, 1913.
[15] Robsmann: Inaug. Diss. Königsberg, 1904.
[16] Von Gossnitz: Jenaische Ztschr. f. Naturwiss. **38**:619.
[17] Kaup: 1891, quoted from Gruber, G.
[18] Gruber, W.: Virchows Arch. f. path. Anat. **47**:382, 1869.

In the case here presented, a male child was born with an uneventful delivery, apparently well nourished and normal, except that the heart beat was well to the right side of the thorax. No pathologic parental history was given.

Attempts to initiate respiration proved unsuccessful, and when artificial respiration, which had been kept up for some time, was stopped, the child, after struggling to breathe, died. Cyanosis was very marked.

Postmortem examination revealed the fact that the diaphragm was entirely lacking on the left side, the left pleural and the peritoneal cavities having wide communication. At the points of attachment of the free edge to the dorsal and ventral body wall it was found to be slightly to the left of the midline. This free edge was thickened to form a heavy muscular band. The thickening indicated, doubtless, that the lateral spread of the diaphragm to the left had been mechanically impaired by the misplaced peritoneal viscera. The phrenic nerves were present on each side in their normal position, the right innervating the right side of the diaphragm and the left being distributed to the thickened muscular band of the free edge.

The diaphragmatic defect can be explained as an arrest of development. The fusion of the splanchnic mesoderm surrounding the left omphalomesenteric vein with the somatic mesoderm of the body wall did not extend as far laterad as normally, and as a result, that portion of the diaphragm derived from the left side of the septum transversum is represented only by the thickened muscular band along the free border, which is innervated by the left phrenic nerve. The left lobe of the liver, also associated in development with this portion of the septum transversum, is reduced in size. In addition to this the left pleuroperitoneal membrane has failed entirely to develop, leaving the left pleuroperitoneal duct widely open. This latter developmental failure may be in some way related to the partial failure of the septum transversum, to the atypical condition of the left duct of Cuvier, or to an anomalous condition of the left mesonephric ridge, or to a combination of such conditions, all of which are associated with the development of the pleuroperitoneal membranes.

This large diaphragmatic defect, as should be expected, was associated with a great change in position and relations of the peritoneal viscera. The esophagus pierced the diaphragm just to the right of the thickened free border, the cardiac end of the stomach, therefore, being in its usual position. The fundus of the stomach, however, had pushed itself forward through the defect into the left pleural cavity, its longitudinal axis being obliquely cephalocaudad, with the greater curvature cephalolateral, to the left, the spleen being situated along the greater curvature. The position of the pylorus was somewhat cephalad of the cardia. The duodenum was attached by a short mesentery to the dorsal body wall, instead of being bound down to it as normally. Its course was not unusual. The jejunum and ileum were not of special interest except that they were crowded to the left and forward so that the jejunum lay entirely within the left pleural cavity (Fig. 1).

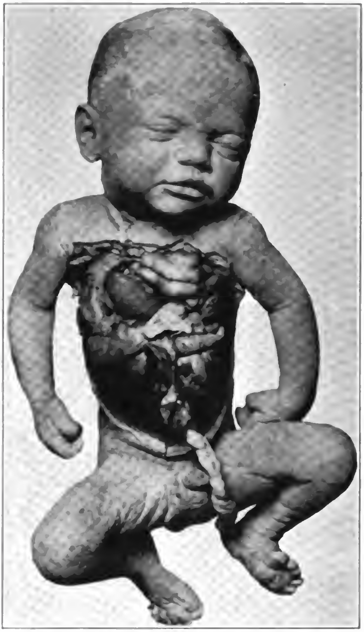

Fig. 1

The colon was also considerably misplaced. The ascending mesocolon was very short and was not fused with the dorsal body wall, so that the ascending colon was not bound down to the body wall, and its position, as was that of the caecum and appendix, was near the midline. The lack of fusion of the ascending mesocolon with the body wall accounts also for the looser binding of the duodenum to the body wall. In its course the ascending colon ran caudally, then describing a U curve ran cephalad to a point just below the free edge of the diaphragm. From here the transverse colon coursed obliquely to the upper left portion of the left pleural cavity, bent sharply, and ran caudally along the lateral body wall. At a point opposite the free edge of the diaphragm it became bound down to the body wall and was considered as the descending colon. The loops of the sigmoid colon were extremely large, and together with the somewhat hypertrophied liver and the rectum completely filled the right half of the peritoneal cavity (Fig. 2).

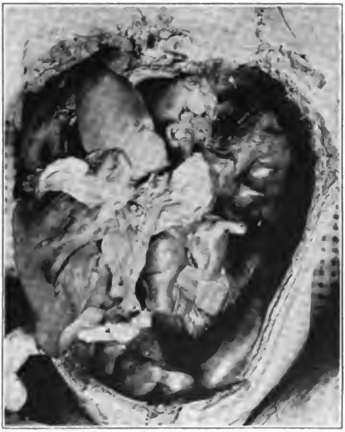

Fig. 2

The liver was somewhat atypical. The right lobe was normal in position, but possibly a little hypertrophied. The left lobe was subnormal in size and the greater part of it was located above the diaphragm in the left pleural cavity, the muscular band of the free edge forming a deep groove on its cephalic surface. The blood circulation of the liver had evidently not been interfered with.

The presence of these peritoneal viscera in the thorax had greatly influenced the development and position of the thoracic viscera. Only a vestige of the left lung was found as a small flap of tissue in the upper central portion of the left pleural cavity. This cavity was greatly increased in size, crowding the mediastinum, thymus, and heart considerably to the right, thus accounting for the fact that the heart beat was felt on the right side of the thorax. This displacement had so decreased the size of the right pleural cavity as to impair the function of that lung. The entire peritoneal portion of the alimentary tract was distended with gas, although neither intestinal occlusions nor imperforate anus were found, thus further increasing the pressure upon, and interfering with the function of the heart and lungs. These conditions were mechanically incompatible with life, death, in this case, resulting from pulmonary insufficiency, followed by extreme dyspoena and cyanosis (Fig. 3).

Added to these conditions before described, there was found, just above the free edge of the diaphragm and adherent to it by a short strip of connective tissue, a triangular mass of tissue, slightly larger than the vestigial left lung, and resembling it in appearance. Histologic examination of sections of this tissue showed it to be an accessory lung (Fig. 1).

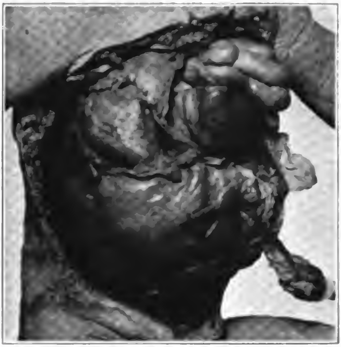

Fig. 3

Cockayne and Gladstone[12] in a review of literature found that in twenty-nine cases in which accessory lungs had been reported, seven of these had been associated with congenital diaphragmatic hernias. The deficiencies in all these cases were on the left side, and the accessory lungs were also on the left side, three only of the twenty-nine cases indicated accessory lungs on the right side, and in six the accessory structure was subdiaphragmatic. It has been suggested that accessory lungs might be accounted for by the adhesion of portions of the embryonic pulmonary tissue to surrounding parts or organs, from which they draw a blood supply, and then become separated from the parent tissue and grow independently.

This theory seems very plausible in the present instance. The only point of attachment of the accessory lung is by means of this narrow fibrous band to the thoracic side of the thickened muscular edge of the diaphragm. Through this, then, is surely the only source of this vascular supply. Both the adhesion of the embryonic pulmonary tissue to the diaphragm and its separation from the parent tissue could be explained by the unusual mechanical conditions present in the left pleural cavity, due to the diaphragmatic defect. It is apparent, in this case, that the presence of accessory lung is a result of, rather than a cause of the defect in the diaphragm.

The prognosis in all cases of congenital deficiencies of the diaphragm is bad. In 112 of the 127 cases reviewed, the age at time of death was given. Eighty-eight of the infants were either stillborn or died within an hour or two after birth. However, life is not always so abruptly terminated by these conditions, as shown by the following: One case was reported in which the child lived three days (Fischer[19]), one lived four days (Millard[20]), one lived eleven days (Krombholz[21]), one lived two months (Booker[22]), one lived four months (Gilford[8]), one lived six months (Hillier, '61), one lived ten months (Fothergill[23]), one lived eleven and one-half months (Lacher[10]), three lived three years (Textor,[5] Mayes[24] two cases), three lived seven years (Diemenbröck,[25] Textor,[5] Downes[26]), one lived eighteen years (Doberauer[27]), one lived twenty-two years (Rosenthal, Keim and Huguier[28]), one young adult (Beck[29]), one lived thirty-one years (Hess[30]), one lived thirty-three years (Abel[31]), one lived forty-three years (Monks[32]), one lived forty-seven years (Vogel[33]), one lived fifty-seven years (Fry[34]), one lived fifty-eight years (Carson and Huelsemann[35]), and one lived seventy years (Guttman[36]).

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[19] Fischer: Diss. de hern. diaphr., Berlin, 1840.

[20] Millard: Canstatt's Jahrb., 1857, No. 3, p. 203.

[21] Krombholz: Schmidt's Jahrb. **28**:199, 1840.

[22] Booker, W. D.: Arch. Pediat. **14**:649, 1897.

[23] Fothergill: Quoted from Lacher.

[24] Mayes, H. W.: Med. Rec. **97**:713, 1920.

[25] Diemenbröck: Schmidt's Jahrb. **121**:336, 1864.

[26] Downes, W. A.: Ann. Surg. **67**:748, 1918.

[27] Doberauer: Brit. J. Child. Dis. **11**: 1914.

[28] Rosenthal, G.; Keim, G., and Huguier: Bull. Soc. d'Obst. de Par., 1898, p. 147.

[29] Beck, T. S.: Tr. Path. Soc. Lond. **6**:19, 1854.

[30] Hess, J. H.: Quart. Bull. Northwestern Univ. Med. School **7**: 1910.

[31] Abel, K.: Berl. klin. Wchnschr. **31**:84, 1894.

[32] Monks, E. H.: Brit. M. J. **1**:708, 1914.

[33] Vogel, K. M.: Am. J. M. Sc. **145**: 1913.

In many of these instances, especially those in which death did not occur until adult life, the diaphragmatic insufficiency was unrelated to the cause of death, the subjects apparently suffering no inconvenience from this lack. Either the misplaced structures were not enough seriously to disturb the pulmonary and cardiac function, or the unaffected lung had so been able to function as to compensate for the loss of function of the other lung. But in all cases in which death was the direct result of the diaphragmatic defect, cyanosis, accompanied by extreme dyspoena and vomiting were characteristic symptoms. In cases of deaths in early childhood the amount of displacement was usually great enough to force the heart from its normal position (right-sided). Percussion of the thorax gives a tympanic note over the area under which the hollow peritoneal viscera lie. Gas is often formed and gas sounds may be heard in these areas of the thorax. The more violent symptoms are most acute when there is gas content in the misplaced portions of the tube, and are much relieved by the passage of the gas.

However, the diagnosis of diaphragmatic hernia in either the acquired or congenital form is extremely difficult, as shown by the figures of Leichtenstern,[37] the condition being usually not discovered until necropsy. The recent use of the roentgen ray in suspected cases eliminates some of this uncertainty. But as the majority of the congenital cases terminate fatally very shortly after birth, if the diagnosis is made in these, it must be based upon physical conditions, as given above, cyanosis, dyspoena, and possible vomiting, associated with atypical chest sounds, abnormal position of the heart, and unsuccessful attempts at respiration. It is very possible that congenital deficiencies of the diaphragm terminating fatally are more common than is indicated by review of the literature, many, doubtless, not having been discovered because of the extreme difficulty of the diagnosis.[38]

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[34] Fry, F.: Montreal M. J. **24**:101, 1895.

[35] Carson, N. B., and Huelsemann, L.: Lancet, 1912, No. 1.

[36] Guttmann, P.: Berl. klin. Wchnschr., 1893.

[37] Leichtenstern: Berl. klin. Wchnschr., 1874, p. 497.

[38] Balfour, F. M.: Edinburgh M. J., 1869.

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EXPERIMENTAL PYLORIC STENOSIS *

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AND
M. A. BERNSTEIN, M.D.
CHICAGO

The pathology of congenital hypertrophic pyloric stenosis is definitely known. The pathologic physiology is still a matter of dispute. Some believe that the symptoms are due to the mechanical obstruction of the tumor itself. Others hold that spasm is responsible for the manifestations of this condition. Both factors probably are operative. Whatever view is held, the picture of pyloric stenosis is easily explained. Narrowing of the pylours, anatomic, spastic, or both, obstructs the passage of food from the stomach. All the symptoms may be referred to that single fact. In order to force the contents beyond the pylorus, gastric peristalsis is exaggerated. This proceeds until the waves show through the abdominal wall running from cardia to pylorus. Visibility of the contractions is enhanced by the diminished tone and atrophy of the musculature of the abdominal wall, due to the virtual starvation which accompanies the condition. The pyloric tumor may be palpated, particularly when the peristaltic wave reaches it. Vomiting occurs because the increased intragastric tension produced by the strong stomach contractions forces the contents through the more patent cardiac end. With the pylorus occluded, the feedings are projected through the mouth and nose. When the peristaltic waves become vigorous, distress is often manifested by the infant. Hunger stools, consisting of thin, green, slimy passages, and constipation occur because little food passes the pylorus. Loss in weight results.

The Rôle of Spasm.—Spasm is considered in the etiology as well as the symptomatology of hypertrophic stenosis. Because snakelike contraction waves are seen passing over the surface of the tumor on operation, some observers attribute the hypertrophy to this constant activity. Facts indicating that these contractions are caused by the tumor will be furnished later.

The symptoms of pyloric stenosis have been ascribed to spasm of the pylorus because relief has frequently followed thick cereal feeding and atropin administration. However, thick cereal is more difficult to eject than fluids. Furthermore, atropin does not exert a selective action

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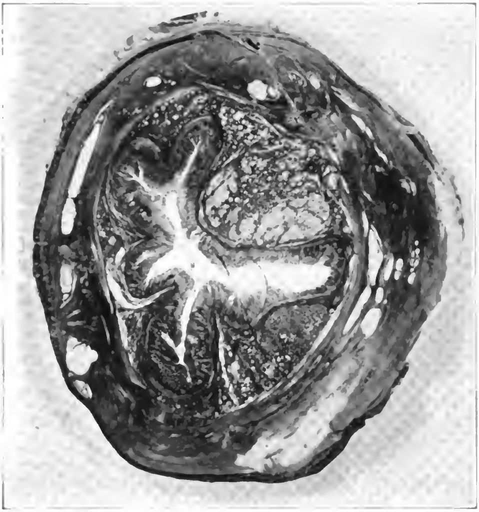
* From the Department of Physiology of the Loyola University School of Medicine.

on the pylorus. It paralyzes the vagus endings with depression of all peristalsis of the stomach. In this way it overcomes spasm from extrinsic causes; for instance, the pylorospasm due to gallbladder and appendix disturbances. On the other hand, atropin has no effect on the spasm from intrinsic causes due to local pathologic conditions.[1] Spasm which may be associated with the usual pyloric tumor of infancy will be unaffected by atropin. Gastric peristalsis may be depressed so that one or more feedings are retained only to be vomited in large part at a later time.



Section through pylorus showing paraffin in the submucosa subdivided by connective tissue strands and thickened muscularis. Note the narrow lumen and infolding of the mucosa. The condition was more marked before the shrinking due to fixing the tissue. × 3.

The Present Problem.—The anatomic condition of hypertrophic pyloric stenosis was imitated by the production of an intramural tumor in the pyloric region in order to determine the effect of pure mechanical obstruction. This angle was chosen because the medical treatment proceeds against the spasmodic factor and the surgical treatment by the Strauss or Rammstedt operation corrects both anatomic and nervous conditions by splitting the tumor and interfering with the nerve supply of the region, particularly in the plastic modification of Strauss.[2]

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[1] Carman: J. A. M. A. **66**:1283 (April 22) 1916. Ivy: Arch. Int. Med. **25**:3 (Jan.) 1916.

Paraffin was used with a melting point of 55 C. and a solidifying temperature of 42 C. Six dogs were employed. Under ether anesthesia an incision was made in the right rectus muscle and the pylorus delivered. The paraffin was injected into the muscularis in quantities of from 8 to 15 c.c. Several points were injected to effect an annular distribution of the material so that a marked anatomic obstruction might be obtained. The paraffin was boiled and slowly cooled to 45 C. This gives an homogeneous liquid which does not solidify until injected. If cooling is rapid the paraffin solidifies in the syringe or needle before it can be properly injected. A large bore needle must be used

The animals were observed as long as seven months. Vomiting was noted. The emptying time of the stomach was studied and compared with normal animals. Gastrostomy was later performed, and stomach tracings taken and compared with normal animals. Finally, the animals were examined post mortem, and the anatomic condition studied grossly and microscopically.

Results.—Immediately after the paraffin was injected, a glistening, white mass was produced resembling remarkably the pale tumor ordinarily seen in the human subject. Still more striking was the appearance of the typical snakelike contractions over this area, later running down the duodenum and toward the antrum. The contractions were observed as long as the region was in view. It should be noted that all the animals had been given $^1/_{150}$ grain of atropin and $^1/_6$ grain of morphin subcutaneously about one half hour before the actual injection.

Vomiting only occurred the first and sometimes the first two days after operation. Following this there were no periods of vomiting with measured amounts of food and, later, the regular feedings of the normal dogs.

The emptying time was studied by administering measured quantities of food and producing emesis by the subcutaneous injection of $^1/_{10}$ grain of apomorphin. Normal dogs were used as controls. It was found more accurate to secure emptying by this means than by aspiration. A mixture of 50 gm. bread and 100 gm. meat ground together and 200 c.c. of water was given and the residue evacuated in one and one-half hours.

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2. Strauss: J. A. M. A. **71**:807 (Sept. 7) 1918.

Paraffin Animals Gm.	Control Animals Gm.
240	200
220	320
240	260
200	150
220	220

One animal with paraffin in the pylorus, which also had an epigastric hernia, gave a residue of 80 c.c. one hour after 200 c.c. milk was given, while two controls gave 10 and 25 c.c., respectively. This result might well be due to the stasis from the large hernia.

There was some increase in the amplitude of the stomach contractions in the injected animals, although unusual tetanic periods did not occur.

The physical condition of the animal was good. They thrived and were very active. In fact, two of them killed each other fighting.

Postmortem examination revealed swelling of the mucosa overlying the paraffin areas, but there were no findings of ulceration or hyperemia. Dilatation of the stomach was not noted. Section showed the lumen almost closed. The mucosa was thrown into folds resembling the clinical species (Fig. 1). The muscularis about the paraffin areas was somewhat thickened. Glistening particles of paraffin appeared in the submucosal region where the injection had bulged the mucosa into the lumen. Microscopic section showed that trabeculae of connective tissue had apparently invaded the paraffin mass subdividing it into smaller particles. The fibroblasts assumed an epithelial like appearance and arrangement so that thinner sections resembled carcinoma. Closer examination revealed the true character of the young, deeply staining cells. There were no giant cells.

SUMMARY

1. The anatomic condition in congenital hypertrophic pyloric stenosis may be reproduced by the injection of paraffin.

2. The picture of pyloric stenosis is not produced. (*a*) Vomiting is only temporary. (*b*) Emptying time is not conspicuously retarded. (*c*) Stomach contractions are moderately increased. (*d*) Stools are normal. (*e*) Emaciation does not occur.

3. It is probable that the snakelike contractions over the surface of the tumor are the result of the muscular hypertrophy in infants, because the injection of paraffin reproduces these peculiar contractions almost immediately and quite constantly. It may be stated, therefore, as a matter of speculation that the tumor of hypertrophic stenosis acts as a foreign body and tends to cause local contractions. The similarity to fibroid tumors of the uterus is immediately suggested.

4. It appears from the failure to produce obstructive symptoms despite marked anatomic obstruction that the clinical picture of hypertrophic pyloric stenosis is not due to the anatomic condition, alone. This agrees with the clinical findings, in which the tumor is usually unilateral and rarely annular.

We wish to thank Dr. A. C. Ivy for his valuable suggestions and assistance during the course of this work, and Dr. Edwin G. Kirk of the Postgraduate Hospital and Medical School for special pathologic preparations.

THE FOOD REQUIREMENTS OF CHILDREN

V. PERCENTAGE DISTRIBUTION OF CALORIES *

L. EMMETT HOLT, M.D., AND HELEN L. FALES
NEW YORK

In the preceding articles in this series we have discussed the total caloric need of the average healthy child and the amounts of the different food constituents—protein, fat and carbohydrate—which should make up the diet. The next point to be considered is the relation of these food constituents to each other and the relation of each to the diet as a whole; in other words, the percentage distribution of the total calories into those given as fat, as protein and as carbohydrate.

In order to determine the usual relation of the constituents of the diet, we have calculated the percentage distribution of the calories in the diets of the 106 healthy children from 1 to 18 years of age studied by us. The values thus obtained for the individual observations are shown in Chart 1. The proportion of the total calories taken as protein is shown at the bottom, that as fat in the middle and that as carbohydrate at the top.

It is evident that the proportion of the calories taken as protein shows the least variation. The average value for all the cases, regardless of age, is 15 per cent. The range is from 11 to 23 per cent., while more than one-half the values are between 14 and 16 per cent.

The per cent. of the total calories taken as fat varies much more widely. The range is from 21 to 51 per cent., but three-fourths of the values are between 30 and 40 per cent. The average of all the cases is 34 per cent.

The proportion of the total calories taken as carbohydrate also shows wide variation. The range is from 38 to 65 per cent., but three-fourths of the values are between 44 and 55 per cent. The average is 51 per cent.

There was no regular variation with age, although the per cent. of the total calories taken as protein was slightly higher in the early years. This is more clearly brought out in Table 1, which gives the average distribution of the calories according to years.

Although there are fairly wide individual variations, it is evident that in the mixed diet commonly taken by healthy children the calories are distributed with surprising regularity. The average of the values

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* Received for publication, June 14, 1922.

* From the laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital.

obtained in our cases may be assumed to represent the usual distribution of the calories in the diet of healthy children. It seems reasonable to make this assumption, when the large number of cases studied is considered, and when it is recalled that the children observed were not a group under any one supervision, but were children in private families in rather scattered localities. Not all of the children lived in New York City. Several lived in Boston, two in Pittsburgh, one in the South and many in New Jersey and Long Island. Regardless of age, the average distribution of the calories taken was as follows: fat, 34 per cent.; carbohydrate, 51 per cent.; protein, 15 per cent. This may conveniently be expressed in round numbers as 35, 50 and 15 per cent., respectively. Therefore, healthy children were found to take, on the average, practically one-half their calories as carbohydrate, a little more than one-third as fat, and only one-sixth as protein. Since 1 gm. of fat has two and one-fourth times the caloric value of 1 gm. of protein, it is evident that in these proportions the amounts of fat and protein are practically equal, while the amount of carbohydrate is a little more than three times as great as either the fat or protein.

TABLE 1.—AVERAGE PERCENTAGE DISTRIBUTION OF CALORIES TAKEN BY CHILDREN

Age, Years	No. of Cases	Fat	Carbohydrate	Protein
1- 2	7	33	50	17
2- 3	11	33	51	16
3- 4	10	34	49	17
4- 5	12	36	48	16
5- 6	10	33	52	15
6- 7	8	35	51	14
7- 8	5	35	52	13
8- 9	9	34	52	14
9-10	9	34	52	14
10-11	9	32	52	16
11-12	4	38	48	14
12-13	3	37	50	13
13-14	1	34	53	13
14-15	3	32	54	14
15-16	3	33	53	14
16-17	1	36	50	14
17-18	1	37	44	19
Total	106			
Average	...	34	51	15

The total calories needed by a child of average activity at different ages have been estimated by us in a former article.[1] Using the average distribution of the calories given above, the theoretical requirements in fat, carbohydrate and protein have been calculated. Charts 2 and 3 show this distribution of the total daily calories for both sexes throughout the period of growth. Charts 4 and 5 give for both sexes the distribution of the calories per kilo.

Table 2 gives the average daily requirement in grams of fat, carbohydrate and protein calculated according to this distribution. Table 3

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1. Holt, L. E., and Fales, H. L.: Am. J. Dis. Child. **21**:1 (Jan.) 1921.

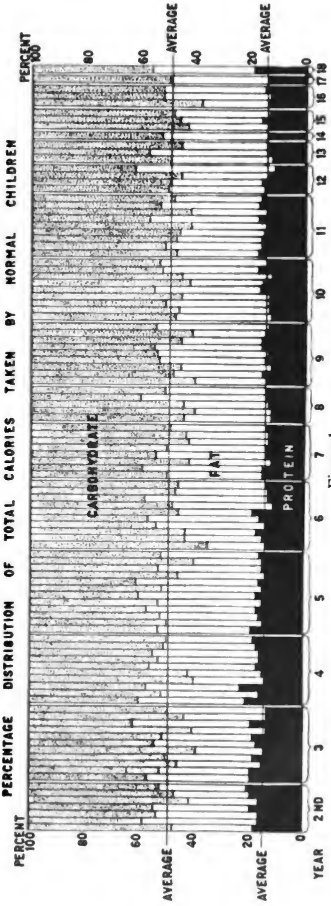
PERCENTAGE DISTRIBUTION OF TOTAL CALORIES TAKEN BY NORMAL CHILDREN
PERCENT
100
80
60
40
20
0
AVERAGE
AVERAGE
CARBOHYDRATE
FAT
PROTEIN
YEAR
2ND
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18

Figure 1

gives the grams per kilo. From these tables it is seen that the results arrived at in this way agree very closely with the estimated requirements of fat, protein and carbohydrate given in the detailed discussion of the theoretic needs for each of these constituents.[2]

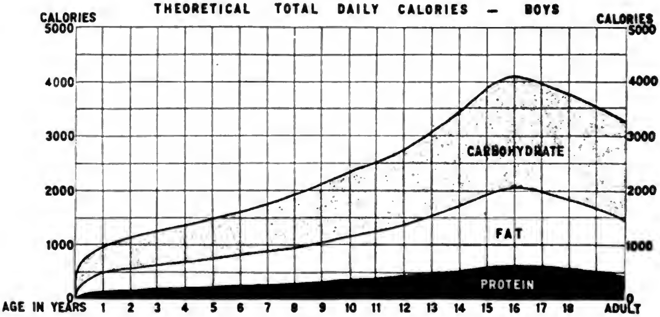

Figure 2

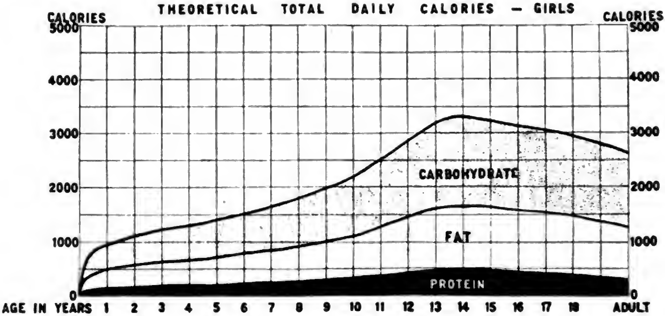

Figure 3

The variation from the average in total calories which are needed by individual children is considerable. This will undoubtedly cause some variation in the distribution of the calories. If the total caloric requirement is increased because of more than average activity, this increase may be met, as has been previously stated, by raising the carbohydrate intake alone. This would increase the proportion of carbohydrate above the average and reduce the proportion of fat and protein, although the amounts of fat and protein remain unchanged. When the total caloric need is lessened because a child is overweight for height or oversize for age, all three constituents of the diet may be reduced proportionally, the normal distribution of calories being retained. This is because the diminished caloric need for growth permits a reduction in the fat and protein as well as in the total caloric requirement. On the other hand, when a child is undersize for age or underweight for height, the total caloric need is greater than the average, and in such cases the usual distribution of calories should be retained, all the constituents of the diet being increased.

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[2] Holt, L. E., and Fales, H. L.: Am. J. Dis. Child. **22**:371 (Oct.) 1921.

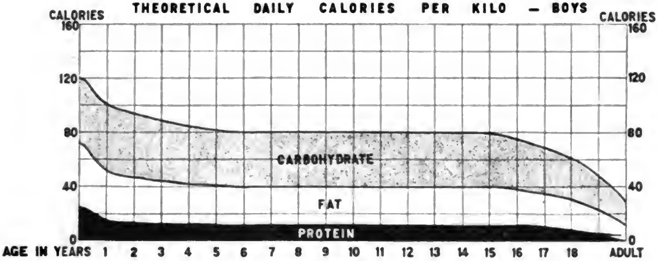

Figure 4

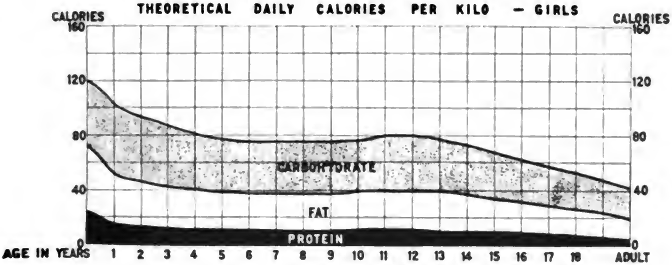

Figure 5

TABLE 2.—THEORETICAL AVERAGE REQUIREMENTS OF HEALTHY CHILDREN—GRAMS DAILY

Age, Years	Boys				Girls			
	Calories, Daily	Fat, Gm. Daily	Carbohydrate, Gm. Daily	Protein, Gm. Daily	Calories, Daily	Fat, Gm. Daily	Carbohydrate, Gm. Daily	Protein, Gm. Daily
1	950	35.8	115.8	35.0	940	35.4	114.7	34.5
2	1,135	42.8	138.3	41.5	1,110	41.8	135.3	40.5
3	1,275	48.0	155.5	47.0	1,230	46.4	150.0	45.0
4	1,380	52.0	168.3	50.5	1,300	49.0	158.5	47.5
5	1,490	56.2	181.8	54.5	1,410	53.2	172.0	52.0
6	1,600	60.3	195.2	58.5	1,520	57.3	184.5	56.0
7	1,745	65.8	212.8	64.0	1,660	62.6	202.2	61.0
8	1,920	72.5	234.2	70.5	1,815	68.5	221.3	66.5
9	2,110	80.0	257.5	78.0	1,990	75.0	242.8	73.0
10	2,330	87.7	284.0	85.5	2,195	82.5	268.0	80.0
11	2,510	94.5	306.0	92.0	2,520	96.0	309.8	92.5
12	2,735	103.0	333.5	100.0	2,865	108.0	349.5	105.0
13	3,040	114.5	371.0	111.0	3,210	121.0	391.7	118.0
14	3,400	128.0	414.8	125.0	3,330	125.5	406.0	122.0
15	3,855	145.0	470.0	142.0	3,235	122.5	394.5	119.0
16	4,090	154.0	499.0	150.0	3,160	119.0	385.2	116.0
17	3,945	148.5	481.5	145.0	3,060	115.5	373.2	112.0
18	3,730	140.5	455.0	137.0	2,950	111.0	360.0	108.0
Adult	3,265	123.0	400.0	120.0	2,640	100.0	322.0	97.0

TABLE 3.—THEORETICAL AVERAGE REQUIREMENTS OF HEALTHY CHILDREN—GRAMS PER KILO DAILY

Age Years	Boys				Girls			
	Calories, per Kg.	Fat, Gm. per Kg.	Carbohydrate, Gm. per Kg.	Protein, Gm. per Kg.	Calories, per Kg.	Fat, Gm. per Kg.	Carbohydrate, Gm. per Kg.	Protein, Gm. per Kg.
1	100	3.8	12.2	3.7	101	3.8	12.3	3.7
2	93	3.5	11.3	3.4	94	3.5	11.5	3.4
3	88	3.3	10.7	3.2	87	3.3	10.6	3.2
4	84	3.2	10.2	3.1	82	3.1	10.0	3.0
5	82	3.1	10.0	3.0	78	2.9	9.5	2.9
6	80	3.0	9.8	2.9	76	2.9	9.3	2.8
7	80	3.0	9.8	2.9	76	2.9	9.3	2.8
8	80	3.0	9.8	2.9	76	2.9	9.3	2.8
9	80	3.0	9.8	2.9	76	2.9	9.3	2.8
10	80	3.0	9.8	2.9	77	2.9	9.3	2.8
11	80	3.0	9.8	2.9	80	3.0	9.8	2.9
12	80	3.0	9.8	2.9	80	3.0	9.8	2.9
13	80	3.0	9.8	2.9	79	3.0	9.7	2.9
14	80	3.0	9.8	2.9	74	2.9	9.0	2.9
15	80	3.0	9.8	2.9	67	2.5	8.2	2.5
16	75	2.8	9.2	2.7	62	2.3	7.6	2.3
17	69	2.6	8.4	2.5	58	2.2	7.1	2.1
18	62	2.3	7.6	2.3	56	2.1	6.8	2.0
Adult	48	1.8	5.9	1.8	44	1.7	5.4	1.6

In animal nutrition much emphasis has been placed on the importance of the "nutritive ratio" which is the relation of the sum of the fat and carbohydrate calories to the protein calories. The publications of the United States Department of Agriculture contain a great deal of information concerning the nutritive ratio which gives the best results in the feeding of animals. It is commonly held, according to Washburn and Jones,[3] that a nutritive ratio of 8: 1 or 9: 1 is proper for mature animals, while growing animals should receive a diet with a nutritive ration of 3: 1 or 4: 1.

The average diet of growing children, having a percentage distribution of calories of 35, 50 and 15, respectively, has a nutritive ration of 5.7: 1. This value falls between that used for young animals and that used for mature animals. To obtain in the diet of young children the nutritive ratio used in feeding young animals, that is, 3: 1 or 4: 1, it would be necessary for the child to take from 20 to 25 per cent. of the total calories as protein. So large an intake of protein is not, according to our observations, usual in the diet of healthy children, and it seems probable that a diet with a nutritive ratio of 5: 1 or 6: 1 provides sufficient protein for the growing child.

Animals grow much more rapidly than children. Furthermore, the normal activity of young animals in most cases equals or even exceeds that of the mature animals. This activity gives rise to a demand for early muscular development. Both these factors, rapid growth and early muscularity, cause an increased need for protein in the diet.

The ration usually considered standard for adults consists of 100 gm. fat, 400 gm. carbohydrate and 100 gm. protein daily. This gives a distribution of the total calories as follows: fat, 31 per cent.; carbohydrate, 55 per cent.; protein, 14 per cent. The average diet of soldiers in the United States Army training camps, as computed by Murlin,[4] had very nearly the same percentage distribution viz: fat, 31 per cent.; carbohydrate, 56 per cent.; protein, 13 per cent. This distribution does not differ very widely from the average we have found in the diets of children, that is, 35, 50 and 15, respectively. The evidence which has been presented, however, shows that children have greater needs for fat and protein than adults. Hence, it seems necessary to supply a higher proportion of fat and of protein than is allowed in the adult ration.

The reports published by other authors of actual diets taken by children show, as would be expected, considerable variation in the percentage distribution of the calories. In most cases, however, the protein taken ranges from 15 to 20 per cent. of the total calories. When the

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3. Washburn, R. M., and Jones, C. H.: Vermont Agric. Exper. Sta. Bull. 195.
4. Murlin, J. R., and Hildebrandt, F. M.: Am. J. Phys. **49**:531, 1919.

total calories were very high, the excess was nearly always in the form of carbohydrate, so that the proportion of protein was low, in some cases as low as 11 per cent. of the total calories. This occurred in the diets reported by Müller [5] and in the average intake of the adolescent boys studied by Gephart.[6]

The proportion of calories supplied by fat in reported diets varies widely but in most cases lies between 30 and 40 per cent. An exception is found in the observations reported by Camerer,[7] in which the fat supplied only from 20 to 30 per cent. of the total calories, while the proportion furnished by carbohydrate was very high, usually between 60 and 65 per cent.

In Camerer's schedule for the feeding of the child throughout the period of growth the proportions of the different constituents of the diet are varied with increasing age. He recommends giving 37 per cent. of the calories as fat at 1 year but reduces the allowance gradually to 23 per cent. at 5 years of age, maintaining this value throughout the remainder of growth. This reduction in fat is met by increasing the carbohydrate. In his schedule, the proportion of carbohydrate rises from 45 per cent. of the calories at 1 year to 60 per cent. at 5 years and remains at this figure throughout the remainder of the growth period. His protein allowance at 1 year supplies 18.5 per cent. of the total calories. The proportion is diminished to 17 per cent. at 5 years and remains at this figure during the remainder of growth. His distribution throughout the greater part of the growth period, therefore, may be expressed as 23, 60 and 17.

The diet schedule for young children suggested by Steffen [8] allows a very high proportion of the calories as fat, more than 50 per cent. up to 3 years and more than 40 per cent. through the seventh year.

Uffelmann [9] suggests for young children diets which have a distribution of calories very similar to our average, the fat a little lower and the protein a little higher. Very few of the other observers who have made recommendations as to total caloric intake have suggested how this should be distributed as fat, carbohydrate and protein.

The conclusion to be drawn from all the observations and discussions presented in this series of articles is the emphasis to be placed on the importance of the balanced ration. We have shown that the protein need of the growing child is very important and there seems to be fairly general unanimity as to the amount required. All evidence seems to indicate that when 15 per cent. of the theoretical total caloric need

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5. Müller, E.: Biochem. Ztschr. **5**:143, 1907.
6. Gephart, F. C.: Boston M. & S. J. **176**:17, 1917.
7. Camerer, W.: Stoffwechsel des Kindes, 1896.
8. Steffen, W.: Jahrb. f. Kinderh. **46**:332, 1898.
9. Uffelmann, J.: Hygiene des Kindes, 1881.

is supplied by protein, the nutritive needs in protein are met. The amount of fat required is still a subject of debate but it seems reasonable and desirable that the amount of fat given to the growing child should be equal to the amount of protein. Since fat has two and one-quarter times the caloric value of protein, equal amounts of fat and protein would supply calories in the proportion of 2.25:1. Therefore, when the protein furnishes 15 per cent. of the total calories, an equal amount of fat would furnish about 35 per cent. The remaining caloric need, that is, 50 per cent. of the total calories, would then be supplied by carbohydrate.

When this distribution is deviated from to any marked degree for a long period, that is, when what seems to be a proper balance of the diet is disturbed, various undesirable results may follow. If the protein is reduced much below 15 per cent. of the caloric requirement, the nutritive need may not be met. If the fat given supplies much less than 35 per cent. of the total calories it usually happens that the carbohydrate intake is excessive and distribution of digestion may follow. If the fat given supplies too high a proportion of the calories the fat tolerance of the child may be exceeded and digestive disturbance may result from the excess of fat. High fat with high protein forms a food combination likely to cause constipation. Low fat with high carbohydrate is apt to cause looseness of the bowels. A large carbohydrate intake means a reduction in the necessary protein and probably equally important fat.

On the whole, one may conclude both from theoretical considerations and from practical observation that a diet in which the fat supplies 35 per cent. of the total calories, the protein 15 per cent. and the carbohydrate 50 per cent., is one which meets the nutritive needs of the child after infancy, which is well borne by the digestive system and may be considered a well balanced ration.

THE USE OF RADIANT HEAT—LIGHT—IN THE TREATMENT OF OTITIS MEDIA *

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CLEVELAND

The great value of the quartz mercury arc ultraviolet ray as a therapeutic measure in various diseases, but especially in rickets, tetany and in certain forms of tuberculosis, has been established beyond question in numerous reports by men of excellent standing, appearing especially in German journals.

As a result a great deal of enthusiasm has been developed for ultraviolet ray therapy and for light therapy in general as well. The latter was responsible for some very interesting work by Oeken [1] on the use of heat rays in the field of otology. To produce these rays, a small, 600 candle power, white glass "Sollux" lamp was used, which is the same, or practically the same, as the higher Watt white glass nitrogen bulbs made in the United States. In the "Sollux" outfit the rays are projected forward and concentrated without causing a burn by the use of a parabolical concave reflector made of aluminum.

Oeken's patients were mainly adults, and he had them sit in comfortable arm chairs during the exposure, which lasted on an average for a full hour. The lamp was placed at a distance of 10 cm. from the ear and the patients were required to wear dark glasses set in leather and tied about the head with strings; in other words, these glasses are devoid of metal in parts that come in contact with the skin for the simple reason that the metal parts might get too hot and might cause a slight burn. Oeken states that in no case did he find any direct harm produced by exposure to the heat rays in the manner described.

He reports his experiences in 258 cases of ear disease, divided as follows: (1) Fifty cases of acute simple otitis media; (2) fifty cases of perforative otitis media; (3) five cases of perforative otitis media with inflammation of the mastoid; (4) two cases of simple mastoid opening; (5) fifty cases of acute otitis media with exudate formation; (6) one case of othematoma and (7) 100 cases of external auditory canal furuncles.

In the fifty cases of acute otitis media with exudate formation he used, whenever possible, the heat rays in an energetic fashion by having

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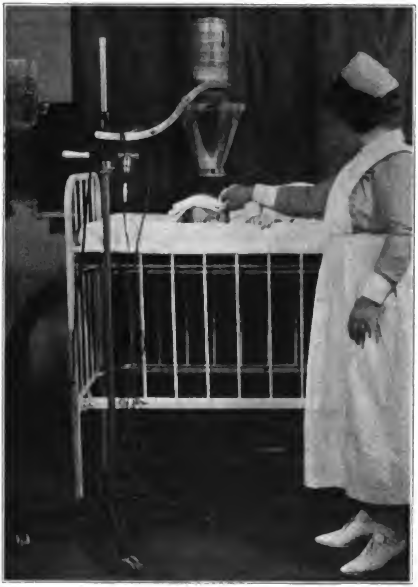
* Received for publication, June 14, 1922.

* From the Department of Pediatrics of Western Reserve University and the Babies' Dispensary and Hospital of Cleveland.

[1] Oeken, W.: Die Anwendung der Wärmestrahlen in der Ohrenheilkunde, Therap. Halbmonatsh. **34**:661 (Dec. 1) 1920.

his patients take daily two sittings of one hour each. He states that after the first exposure the earache was markedly lessened and the patients felt better generally as well. In most cases the drum membrane cleared up within two to three days, the exudate was absorbed and the bulging of the membrane disappeared. Whatever deafness remained was soon relieved by using the air douche. In all the fifty cases he was able to control the infection and avoid a paracentesis. From four to ten exposures were necessary. He emphasizes that in these cases the ideal result for otologists is the complete restoration of the drum membrane to a normal state without scar formation, and he maintains that the heat rays are a most important aid in accomplishing this object.



Showing child being exposed to rays from Sollux lamp with towel over side of face to protect eyes. Lamp 10 cm. from ear. Duration of exposure, one hour; once or twice daily.

Oeken goes on at this point to state that he began the use of the heat lamp with a great deal of pessimism, but after his experience with it he is convinced that without its use, in at least one third of the cases just discussed, a paracentesis would have been necessary. He writes that in his opinion, in addition to the marked analgesic effect that follows even the first exposure, the avoidance of the painful paracentesis in these cases of acute otitis media with exudate formation will insure its permanent place as a welcome therapeutic measure.

In his group of fifty cases of acute perforative otitis media, Oeken has included only those patients who came to him with the drum membranes already perforated. The course of treatment in these cases was as follows: (1) Cleansing of ear canal before exposure to light; (2) daily exposure to light for one hour at 10 cm.; (3) on an average, after the fifth day, an air douche once daily; (4) the use of hydrogen peroxid three times daily at home.

On an average ten exposures were necessary to cause a cessation of the secretion, the smallest number being three and the largest twenty. In all cases the drum membrane was completely healed and no deafness remained, and with these cases Oeken had the same good results in stopping earache and improving the general well being of his patients that he had with the other group. In one of his cases the difference between his own treatment without the lamp, on the one hand, and with the lamp, on the other, was especially made clear. This patient had come to him once before with a bilateral purulent otitis media which required four weeks of treatment, during the first two of which pain and discomfort were present. During the second attack of perforative otitis media, the regular treatment was augmented by the use of the heat rays, with the result that the earache disappeared immediately, the patient felt better generally, and after the eighth day he was able to work again. He states that the other forty-nine cases followed a similarly good course. Oeken admits, however, that with the exception of the clear cut and rapid disappearance of earache following the use of the heat rays it is, of course, difficult to judge in an objective manner the exact degree of improvement produced in these cases by the light rays inasmuch as many cases of perforative otitis media also clear up without their use. Nevertheless, he has the decided impression that since he has been using the light therapy this type of otitis media has been milder in degree and shorter in duration.

In the care of other groups of cases Oeken likewise has experienced beneficial results with the use of the heat rays, but it would lead us too far to discuss these here. His general conclusions, however, as to the results obtained with the use of the heat rays in the type of cases under consideration are as follows: (1) Immediate removal of all pain.

(2) Marked resorption of exudates and as a result a lessening of the duration of the infection and a tendency to prevent pus formation. (3) A decrease of the necessity for operative interference—paracentesis and mastoid opening.

How are these results brought about? Oeken's opinion is that the remarkable hyperemia which is produced deep down in the tissues and which persists for hours is responsible. The well known healing power of hyperemia is more intense when produced by the heat rays and remains for a longer period than that produced by other methods of heat application. Whether any additional specific characteristics of the heat rays exist and operate in the production of this improvement Oeken states is still an unsettled question.

Our own plan in trying out the treatment of otitis media with heat rays according to Oeken was to use them, following his directions, in two types of cases: (1) chronic suppurative otitis media and (2) early scarlet fever and measles showing normal drum membranes to see whether the development of otitis media in these diseases could be lessened. In this latter series an untreated case was to alternate with a treated one. The second plan, however, did not progress very far because of our inability to get adequate assistance in applying the light. The lamp was there long enough, however, to prove to the adult patients that it had a marked analgesic effect and as a result some of the attendants, without our permission, exposed sore fingers and the like to the rays.

In this report, therefore, are included only our experiences with ambulant cases of chronic otitis media coming to the Babies' Dispensary. Observations on five such cases were also made at one of the hospitals, but inasmuch as here, again, it was impossible to find sufficient help to see that the light was properly applied, these results are not included here. In the case of the ambulant patients coming to the Babies' Dispensary the mother who brought the patient was able to sit at the table and keep the child in the proper position and in this manner insure an exposure to the heat rays as ordered.

The plan of treatment was as follows:

(1) Cleansing of the external canal of any pus that was present when the exposure was to begin.

(2) Exposure of the ear to the light for one hour at a distance of 10 cm. The infants and children were placed on a table with the ear to be treated up. Dark eyeglasses, such as Oeken used, were applied, or the mother held a small towel over the face in front of the ear and in this manner protected the eyes.

(3) Cleansing of the external auditory canal with hydrogen peroxid at home three times daily.

(4) Return for exposure to light once daily, except Sundays. This part of the treatment was carried out as desired only in a certain number of cases. Bad weather and lack of realization by the parents in others caused some irregularity in attendance.

All of our patients had discharging ears for a period of four weeks or more. Thirty patients reported for one or more treatments. Of these sixteen stopped coming before a cure was effected, that is, complete cessation of the discharge and healing of the drum membrane. The facts concerning the latter are as follows: One left town. One was referred to a hospital for mastoid operation which, however, was never performed. One and one-half months later the discharge stopped. Two developed measles. The ears of one of these patients, however, had healed when he returned to the dispensary fifteen days later. Two showed an incomplete cessation of the discharge, one after six treatments and the other after twenty-two treatments. In two no external discharge was present at the last visit, but the drum was still perforated and moist. Eight, no cause.

Of the fourteen who continued to come, eleven were cured and by this we mean not only a cessation of the discharge, but also a healing of the perforation in the drum membrane. All of these cases showed a lessening of the discharge within two or three days. External excoriation disappeared simultaneously. Not only objectively but subjectively was there early and decided improvement. The most marked effect in infants is the change of disposition. The fretful, restless baby becomes happy and quiet after the first treatment. It sleeps better at night and its appetite improves. There is no doubt in the minds of the mothers about this, and this is an absolute corroboration of Oeken's finding.

To produce a cure, ninety-six exposures were required for the eleven cases, or an average of 8.7 per patient. The smallest number of exposures was two, and the largest fourteen. For the individual cases the number of exposures was as follows: 2; 4; 5; 5; 8; 8; 11; 12; 13; 14; 14.

When we consider that all of these children before treatment had discharging ears for four weeks or more and were uncomfortable during the same time, the rapid improvement in local and general discomfort and the healing of the drum membrane after a maximum number of fourteen exposures is remarkable and gratifying.

Three of the fourteen patients are still coming. One of these is a relatively recent case and is improved, while the other two are extremely chronic cases, the one having had a discharging ear for eight years and the other for five years. The latter has shown a little improvement in that there is no external discharge. Through a large opening in the drum membrane, however, thick, purulent material can still be seen. Thirty-two light treatments so far have been given this patient without causing a cessation of the discharge; in other words, this is a refractory case.

The former very chronic case is a colored boy in whom both membranes have been destroyed. When he came to us he was avoided at school on account of his foul aural discharge. For the past year he had been attending a nose and ear clinic once or twice per week. He showed a rapid improvement after the fifth treatment. After the nineteenth exposure to the heat rays all discharge had ceased in the right ear, while the left ear, which had not been treated with the light, showed no improvement. The left ear then was treated and ceased discharging after the sixth treatment. The right ear had a total of thirty-two exposures and the left a total of ten. Inasmuch as the drums are gone, we are continuing the light therapy twice a week for an indefinite period even though the ears have been completely dry for quite a time. A similar observation was made in one of the eleven cases mentioned above. In this case the light treated ear ceased to discharge while the untreated ear did not. In another case, however, which was temporarily treated at one of the hospitals and which is not included in this report, the opposite result was obtained, namely, the light treated ear continued to discharge while the untreated ear ceased discharging. Whether this was a coincidence, or whether it was due to a reflex hyperemia or to some other cause, we do not know.

In picking out our patients to be treated with the heat rays, we intentionally took the seemingly refractory chronic cases of purulent otitis media because we felt that a decided improvement in these cases after the use of the heat rays would really be of objective value, and it seems to us that we have obtained such a result and, therefore, we are in complete agreement with Oeken's findings and conclusions for this group of cases.

When one has used such a lamp and has seen the intense hyperemia produced by it without any discomfort to the patient—many infants sleep during the exposures—one realizes its great effectiveness and simplicity, and also its superiority over the contact method of applying local heat through the use of pads, bags and packs; and this difference is understandable when it is appreciated that the effective rays emitted from these lamps have relatively long wave lengths and, consequently, possess a great ability to penetrate deeply into the tissues where this light energy is transformed into heat energy with a resultant vasodilatation and hyperemia. The local hyperemia produced by pads, bags and packs is much more superficial.

The actinic rays, or ultraviolet rays, of course, can play no part in the therapeutic result obtained in these cases for the reason that the relatively few that are produced by a nitrogen lamp cannot pass through the glass used in the manufacture of the bulb. Whether, however, the rays of longer wave lengths, especially those on the red and infra-red side of the spectrum, have any further specific effect in addition to this power of causing the deep hyperemia by deep penetration, remains at present an unanswered question. There are men who believe that the red and infra-red rays have a specific therapeutic property, and Thedering[2] especially is of this opinion. He has offered a hypothesis which postulates among other things the idea that the red and infra-red rays balance, as it were, the violet and ultraviolet rays.

CONCLUSIONS

On the basis of our experience in treating persistent chronic cases of otitis media in infants and children with radiant heat—light—as discussed above, we feel justified in concluding as follows regarding their therapeutic value:

1. Local and general discomfort are in most cases removed after the first exposure.

2. Virtually all cases show not only a cessation of the discharge, but also a complete healing of the drum membrane.

3. On an average 8.7 exposures—from two to fourteen in the extremes—were sufficient to bring this result about.

4. Without question radiant heat in the form of light is a therapeutic measure of great value, which will be found useful not only in the treatment of otitis media in its various forms but also in other conditions in which the therapeutic effectiveness of an active hyperemia is desired.

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[2] Thedering: Versuch einer theoretischen Begründung der Rotlichttherapie, München. med. Wchnschr. **67**:1919 (Sept. 24) 1920.

INFANTILE RICKETS: THE SIGNIFICANCE OF CLINICAL, RADIOGRAPHIC AND CHEMICAL EXAMINATIONS IN ITS DIAGNOSIS AND INCIDENCE *

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It is difficult, indeed impossible, as will be shown later, to state categorically the incidence of rickets. In large cities this has been variously estimated at from 50 to 75 per cent. or more among artificially fed infants. In the course of caring for a large group of young children in a model institution, situated in the outskirts of the city, it occurred to us some years ago to inquire how frequently rickets developed under these favorable conditions. It seemed especially worth while to ascertain, by careful and continued observation, whether this disorder came about with the same frequency among these infants as among the infants in the average city home. Our group has comprised about 250 babies less than 18 months of age, who have been cared for during the past four years. A group of this kind, living under similar hygienic surroundings, and receiving at all times a carefully regulated diet, prepared in a central diet kitchen, presents an exceptional opportunity to follow nutritional conditions and particularly to observe disturbances at their earliest beginning. The babies were almost all of Russian Jewish parentage, a stock which is considered not peculiarly susceptible to rickets, or to other nutritional disturbances. All were free from clinical symptoms of syphilis and gave a negative Wassermann reaction—a test which, however, is of limited value at this time of life. Their diets were those most commonly used—pasteurized milk, dried milk, raw certified milk, given either in simple dilution or in special formulas.

In order to lend uniformity to the data, these examinations, some two thousand in all, were performed by the same person almost throughout the entire period. This survey included notation of the weight, shape of the head, craniotabes, presence of teeth, bowing of legs and curvature of the spinal column, beading of the ribs, tonicity of the muscles, umbilical hernia, diastasis recti, enlargement of the spleen, etc. About three years ago monthly roentgenograms of the lower epiphyses of the ulna and radium and of the carpal bones became part of the routine examination, and for the past year a monthly analysis of the blood has been made, especially for its percentage of

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* From the Home for Hebrew Infants.

inorganic phosphate. It is these cases in which clinical, radiologic and chemical tests were carried out to which we shall devote particular attention. Most of the infants have been followed month by month for from six to twelve months, and many for a year or more. No case has been considered which has been under observation for less than four months.

In spite of these improved diagnostic methods, the recognition of rickets has become increasingly difficult, due to our realization of the complexity of this disorder. It is more and more evident that there is no pathognomonic sign, no sign which can be accepted as invariable evidence of the presence of rickets. Among the symptoms frequently emphasized as of value in this connection, are head sweating, inability to sit or to stand at the normal age, delayed eruption of teeth, poor tonicity of muscles. Without entering into a detailed discussion of these phenomena, it may be stated that they all proved unreliable. Head sweating is a symptom of minor importance because it is frequently absent and is by no means specific of this disorder. The age of learning to sit or to stand depends on various other factors. As an example of its lack of dependability, a rachitic breast-fed baby may be cited which sat up well at 6 months of age. This infant showed the distinctive signs of rickets (rosary, enlarged epiphyses, radiographic picture) to greater degree than any infant included in Table 4. It was omitted from this table because it was of Italian parentage. The most significant factor associated with delayed dentition has been, in our experience, not rickets but feeblemindedness. The instances in which mentally backward children did not erupt a tooth until 12 or 15 months of age have been both numerous and striking. In these cases cod liver oil, given for six months, from three to six teaspoonfuls daily, did not induce dentition. On the other hand, there have been numerous cases in which the teeth erupted normally in the course of the development of rickets.

Craniotabes.—On account of the many qualifications with which it is attended, craniotabes must be regarded as an unreliable sign of rickets. In young infants, those under three months of age, there is the difficulty, insurmountable in many instances, of differentiating it from the cranial softening of the newborn, which is not truly rachitic. It has its greatest diagnostic significance somewhat later, after the sixth month of life. It was found at some time in one-third of the babies in our institution. As the incidence of rickets in bottle-fed babies is always greater than this, it is evident that it is not a constant sign. Indeed, in the mild or moderate type of disorder such as we have had under observation, due to the fact that cod liver oil or heliotherapy was begun as soon as the roentgen ray showed any changes, craniotabes was absent more often than present. Its absence, therefore, has no diagnostic significance. By the time the infants arrived at the age of 6 months, or more, this sign was elicited only in 10 per cent. of the cases. In numerous instances the softening healed before, or even in the course of the development of the characteristic radiographic changes, so that had craniotabes been used as a criterion, the rickets would have been considered as cured. This quality, noted frequently by others, of complete healing despite a general advance in the rachitic process renders this sign unsuitable for a standard. Craniotabes has been associated in numerous instances with a normal content of inorganic phosphate in the blood, but frequently with an abnormally low percentage of calcium.

Beading of the Ribs (Rosary).—Of all the direct clinical signs of rickets, beading of the ribs was found to be the most constant and reliable. Attention has been focused more and more on this sign in the 2,000 physical examinations which have been carried out in the course of this study, and lately its time of appearance has been compared with the advent of roentgenologic changes and a diminution in the inorganic phosphate of the blood. Beading occurs not only in rickets but in scurvy,[1] so that it is impossible to interpret its nature when latent scurvy may be present. This question arose in connection with a few cases at the time of admission, but could be disregarded in relation to all other infants, as they received orange juice daily. One cannot state categorically that beading never occurs in other clinical conditions; if it does, it is an exceptional manifestation, for there have been but two or three instances in which it could not be definitely linked with rickets. Six gradations of beading have been formulated, to the mildest of which (±) no significance was attached. Its value is greatest in the second half of the first year of life; during the first half of the second year it frequently becomes obliterated by the recession of the costochondral junctions, leading to the formation of the well known Harrison's groove. Where this groove is present the sign should be disregarded.

Tables 1 and 2 show the occurrence of beading of the ribs in its relation to radiologic changes and diminution of the inorganic phosphate of the blood. In Table 1, composed of three representative cases in which rickets developed on certified raw milk, it will be noted that beading frequently precedes the radiographic evidence, and that it may or may not antedate the chemical alteration of the blood. The third case serves to illustrate the marked distinction between the value of beading for early diagnosis and for beginning cure. This infant was cured rapidly by means of irradiations from the carbon arc lamp. In spite of the pronounced healing clearly shown by the roentgen rays as calcification of the epiphyses, and by an analysis of the blood, the rosary did not diminish in size. This is frequently the case; in fact in some instances the costochondral junctions became more angular and firmer, probably as the result of calcification. Therefore, although beading may gradually disappear under specific therapy, its persistence must not be regarded as indicating failure.

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[1] Hess, A. F., and Unger, L. J.: Am. J. Dis. Child. **19**:331 (April) 1920.

Table 2 represents a comparative study of the first sign of rickets among the fifty-three infants supervised this year. Previous experience had led us to believe that beading of the ribs is a more reliable criterion in this respect than the radiographic picture. It will be seen that among the fifty-one cases of rickets, beading was the first sign in twenty-four instances, and in sixteen instances occurred simultaneously with one or more other signs. This order of precedent, however, may not hold good for every diet and under all hygienic conditions. Rickets, associated with a certain diet, may be characterized by distinguishing lesions. In this respect the divergent histologic pictures may be called to mind which develop in rats fed a low phosphorus and high calcium diet, compared to that resulting from a diet low in calcium and high in phosphorus; the former is characterized by a broad band of cartilage not seen in the latter. Whereas the rickets associated with raw certified milk, or with breast milk, is accompanied by an early enlargement of the costochondral junctions, that associated with a diet of condensed milk has seemed to be characterized by bowing of the legs.

TABLE 1.—INCIDENCE OF SIGNS (RAW MILK)

	December	January	February	March	April
1. Rosary	+	+	+	+±	+±
Roentgen ray	Negative	Negative	Negative	Rickets	Rickets
Phosphorus	3.45	3.31	....	3.28	3.17
2. Rosary	±	+	+±	+±	+±
Roentgen ray	Negative	Negative	Negative	Mild rickets	Mod rickets
Phosphorus	3.22	....	2.94	2.93	2.85
Carbon arc lamp					
3. Rosary	+	+±	+±	± ±	
Roentgen ray	Negative	Mild rickets	Healing	Healed	
Phosphorus	4.00	3.69	4.29	4.25	

TABLE 2.—FIRST SIGN OF RICKETS (51 CASES)

	Dried Milk	Raw Milk	Protein Milk	Total
Rosary	14	9	1	24
Roentgen ray	1	0	1	2
Blood phosphorus	4	2	1	7
Rosary + roentgen ray	1	0	0	1
Rosary + phosphorus	5	2	1	8
Roentgen ray + phosphorus	2	0	0	2
Rosary + roentgen ray + phosphorus	2	3	2	7
Total	29	16	6	51

Roentgenogram of the Epiphyses.—The fact that beading of the ribs is a subjective sign, fluctuating according to the experience or the point of view of the examiner, lessens its value. It might be thought that radiologic examination of the epiphyses is purely objective and, therefore, not open to this criticism. It is true that it is easy to interpret marked rachitic lesions, those characterized by decided cupping of the ends of the bones, especially of the ulna, and by a diminished calcification of the shafts. But in endeavoring to discover early rickets many instances were encountered which led to questioning. Every month in the course of a scrutiny of about seventy-five roentgenograms there have been at least four or five films which could not be diagnosed satisfactorily. If this perplexity exists when previous roentgenograms are available for comparison, as well as a clinical record of the case, how much greater must be the uncertainty when the diagnosis has to be made from a single roentgenogram. The main obscurity has been the pathologic significance of what may be termed "slight spreading" or "spreading" of the ulna. In some instances this deformity has developed later into "slight rickets," in some it has remained stationary although other rachitic signs have developed.

This is merely one aspect which has rendered radiographic diagnosis unsatisfactory and disappointing. A criticism of wider applicability is that the roentgenogram frequently is negative, although beading of the ribs, the diminution of inorganic phosphate, and the general appearance of the infant clearly point to rickets. Table 2 shows that among fifty-one cases the diagnosis was first established by means of the roentgen ray in only two, and that only in ten other instances did it furnish evidence as early as the clinical or chemical tests. A survey of our complete data leads to the same conclusion. Two hundred and forty-four cases have been radiographed month by month by Dr. Charles Gottlieb, comprising almost 2,000 individual photographs. One hundred and forty-nine of these have shown rachitic changes roentgenologically. In how many did the roentgen ray and in how many did beading of the ribs give the first evidence of rickets? In thirty-one cases both appeared simultaneously, so that these must be deducted from the total, leaving 118 as a basis of comparison. In fourteen cases the diagnosis was first established by roentgen ray, and in 104 by beading of the ribs.

How can this comparative precocity of beading be explained? No doubt, it is partly attributable to the fact that we are not comparing the same articulations. The costochondral junctions are involved early in rickets, due probably to the rapid growth of the ribs, and could they be radiographed satisfactorily, the roentgen ray would not be so tardy in diagnosis. In our experience raying of joints, other than the wrist, furnishes still later information. In numerous instances several articulations of the extremities were examined roentgenologically, but in none were lesions seen when the wrist joint appeared normal. There is another aspect which should be referred to. In the course of a general physical examination the epiphyses of the wrist were found enlarged in surprisingly few cases, far less than among the negro babies examined by us some years ago, or in the breast-fed babies represented in Table 4. This sign of rickets is very inconstant and is found most often in well nourished infants. It is of interest in this connection because the wrists may be enlarged to palpation and, nevertheless, be negative to the roentgen ray; in one instance where the epiphyses were distinctly enlarged, repeated roentgenograms were negative. Furthermore, in the great majority of cases in which rickets was diagnosed by roentgenograms of the wrists, the epiphyses apparently were normal in size and contour.

It should be borne in mind that these statements regarding the unreliability of roentgenograms apply solely to early diagnosis. In distinguishing the healing of the rachitic process, the roentgen ray is invaluable and gives evidence far in advance of simple clinical signs. Indeed, in this respect, as stated, beading of the ribs may be absolutely misleading. It is remarkable how quickly the epiphyses respond to specific therapy or to "change of season" by the formation of a more or less intense line of preparatory calcification. This response of the epiphyses to curative agents is so reliable that it has been employed by Mellanby in dogs[2] and by Howland and Park in infants,[3] to demonstrate the specific therapeutic value of cod liver oil.

Centers of Ossification of the Carpus.—The relation of the development of the carpal centers to the early diagnosis of rickets may be dismissed in a few words. The time of appearance of these centers seems to depend primarily on rate of growth, and to be influenced mainly by factors which affect this rate. An exception may be made to this statement in regard to premature infants, which generally show delay in the appearance of the carpal centers. The cases of rickets under consideration, which in most instances were so mild as to escape casual diagnosis, and were detected only by means of refined methods, showed no retardation of growth in weight or in length and likewise no delay in carpal development. As an illustration of the lack of interrelationship between rickets and carpal development, the case of a breast-fed baby may be cited which developed rickets when 4 months of age, although two carpal centers were manifest before she was 2 months of age.

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[2] Mellanby, E.: Medical Research Committee Special Report, Series 38, London, 1919.

[3] Howland, J., and Park, E. A.: Arch. Pediat. **37**:411, 1920.

Inorganic Phosphate of the Blood.—Recently Howland and Kramer[4] reported that the inorganic phosphate of the serum is regularly reduced in infants during active rickets. In the course of the past year this test has been included in the monthly examinations. For this purpose the Bell and Doisy colorimetric method was used, with the modification that paraffined tubes were employed instead of adding oxalate to the blood. The normal plane of inorganic phosphate, as determined by this method, is approximately from 4.0 to 4.8 mg. per 100 c.c. of blood. Percentages of 3.75 mg., or less, were considered within the rachitic range. It would lead too far afield, nor is the time ripe, to discuss in detail the significance of a diminution of the inorganic phosphate of the blood. We have met with cases of undoubted rickets where the blood phosphate was not decreased, and some where it was found to be below 3.75 mg. per cent., and an observation of several months showed no clinical or radiologic evidence of rickets.[5] In one instance of this kind where the diet had been raw certified milk, histologic examination of the epiphysis of the ulna was negative. There are evidently factors other than rickets which tend to a reduction of the inorganic phosphate of the blood. Recent investigations lead to these deductions. In this connection experiments on the rickets of rats should be borne in mind, which clearly show that although low inorganic phosphate of the blood generally accompanies rickets, the diet may be so constituted that the inorganic phosphate is greatly diminished and yet rickets not result. Hess and Lundagen[6] have shown that there is a marked seasonal tide in relation to the inorganic phosphate of the blood, that in almost all infants there is a tendency for this constituent to fall gradually during the winter months, reaching its lowest ebb in March, gradually rising to its flood in the summer season.

In spite of these factors, rickets seems to be the most important clinical disorder associated with low phosphate, and although the test cannot be considered pathognomonic of rickets, it is of distinct value in early diagnosis. The percentage of phosphate seems to bear some relation to the nature of the diet, a diminution coming about more often and earlier on dried milk or on protein milk than on raw milk. It cannot, however, be brought back to the normal, or regularly increased by adding large amounts of phosphate to the dietary (K_2HPO_4, 2 gm. daily). Table 2 shows that in seven of fifty-one cases this sign preceded all others, and that in seventeen other instances it was noted simul-

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4. Howland, J., and Kramer, B.: Am. J. Dis. Child. **22**:105 (Aug.) 1921.

5. In three cases of this kind cod liver oil was given for one month, from March 20 to April 20, and brought about decided increases in the inorganic phosphate of the blood: from 3.58 mg. to 4.03 mg., from 3.03 mg. to 4.21 mg., from 3.55 mg. to 4.11 mg.

6. Hess, A. F., and Lundagen, M.: Proc. Soc. Exper. Biol. & Med. **19**: 1922.

taneously with one or other signs. It is, therefore, to be regarded as an early phenomenon of rickets. Unless a consecutive series of tests is available for comparison, an analysis showing low inorganic phosphate does not indicate whether the rachitic process is healing or advancing. When, however, previous figures are at hand, this test generally will be found of value in judging the trend of the disorder. It cannot be relied on in this regard. Instances have been encountered in which roentgenograms showed healing and the inorganic phosphate had increased but little; for example, cod liver oil was given to an infant from May 12 to June 13 and the inorganic phosphate rose only from 3.33 to 3.54 mg., whereas the roentgen ray showed definite healing. The most reliable criterion of healing is the roentgenogram.

THE INCIDENCE OF RICKETS

As stated, there are no reliable statistics of the incidence of rickets. This is true of urban and of rural communities, but especially so of the latter. Various approximations have been made—some years ago by Kassowitz, more recently by Findlay and by Thompson, and for colored infants by Hess and Unger—all based on estimations or on simple physical examinations. No attempt has been made to use the roentgen ray to obtain more accurate data. Nor has any inquiry of this kind been confined exclusively to a short period of the year, for example, to one or two of the winter months, when rickets flourishes. The test of the blood for inorganic phosphate is, of course, too recent an innovation to have been employed for this purpose.

TABLE 3.—Incidence of Rickets Under 18 Months
221 Necropsies (Schmorl)

Number of Children	Age, Months	Total Rickets		Rickets Absent	
		Cases	Per Cent.	Cases	Per Cent.
34	4- 6	33	97	1	3
53	7- 9	50	94	3	6
75	10-12	73	97.3	2	2.7
59	13-18	58	98.3	1	1.7
221	.....	214	96.7	7	3.2

To our knowledge there is but one study of the incidence of rickets from a pathologic point of view—that of Schmorl [7]—a routine investigation of cases as they came to necropsy for one cause or another. A study of this kind has the great advantage of being able to discern, and therefore to include, active as well as inactive, incipient as well as healed rickets. A table has been prepared summarizing part of this investigation (Table 3), namely the data bearing upon 221 necropsies made on infants under 18 months of age, the age period embraced by our study. On consulting this table it is seen that more than 96 per cent. of the infants showed lesions of rickets and that histologic changes were absent in only seven of the 221 cases.

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[7] Schmorl, G.: Ergebn. d. inn. Med. u. Kinderh. **13**:403, 1914.

In a clinical study the percentage of rickets will depend to a far less extent on the diet of the infants than on incidental factors. It will vary greatly according to the variety of the diagnostic methods and the care and understanding with which they are employed, and also according to the season or even the month of the year when the examinations are carried out. All agree that the diet in which rickets develops least often is breast milk. In order to ascertain its incidence on this diet, a careful examination of twenty-five breast-fed infants, similar in nationality to those in our institution, was carried out in a baby welfare station. A glance at the weight in relation to the age of these babies—varying from 4 to 10 months—shows that they were an exceptionally well developed group[8] (Table 4). The test for inorganic phosphate was omitted. The result of this study is reproduced in the table. It will be noted that ten babies, or 40 per cent., showed rickets by roentgen ray, nine had decided beading of the ribs (+), and seven had craniotabes. Leaving craniotabes out of consideration, and including only such cases as showed rickets either roentgenologically or by beading, it is found that thirteen of twenty-five, or more than one-half, had rickets. This high percentage may seem surprising. It is due to the fact that the investigation was carried out at the end of March, a time when every potential case of rickets had developed and none had undergone spontaneous cure. Most of these infants had to depend on breast milk to protect them from rickets and were deprived of the powerful adjuvant of sunlight. In this respect breast milk is not endowed with a marked factor of safety.

Our experience with bottle-fed babies coincides in general with the pathologic report of Schmorl.[7] If the most refined tests are employed and careful examinations are carried out at a time when the incidence is highest, almost all artificially fed infants will be found to have a certain degree of rickets. This, of course, does not apply to the exceptional infant who receives an abundance of sunlight.[9] This year, at consider-

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[8] In view of the theory which suggests a lack of fat soluble vitamin as the determining factor in rickets, it may be remarked that the mothers also were well nourished. Many of them consumed a quart of milk a day; on account of religious scruples they do not eat oleomargarine but only sweet butter. In this connection reference may be made to a breast-fed infant in our institution which developed rickets. It was the baby of a wet nurse whom we know to have been on a liberal diet which included fresh vegetables and one or two quarts of milk daily.

[9] Nor does it apply with equal force to the baby born in the winter, and who at the end of March—the peak of the rickets season—is but 3 or 4 months of age. It has seemed that infants born about the beginning of February were least likely to develop rickets; they are subjected to only a few months of lack of sunlight and then enjoy a prolonged period of intense sunlight. Under ordinary conditions rickets does not develop after the beginning of May.

TABLE 4.—INCIDENCE OF RICKETS IN MARCH AMONG 25 BREAST FED INFANTS (BABY WELFARE STATION)

Case	Age, Mos.	Weight, Lbs.	Condition	Head	Fontanelle, Inches	Craniotabes	Teeth	Rosary	Epiphyses	Bow Legs	Sits	Pot Belly	Diastasis Recti	Umbilical Hernia	Muscles	Spleen Palpable	Radiograph		Remarks
																	Epiphyses	Carpal Centers	
1	6	13-14/16	Good	......	2 × 2	+	0	+	0	+	0	0	+	0	Good	0	Rickets	2	
2	9	21- 2/16	Good	......	1 × 1	0	4	0	0	0	Sits	+	+	0	Good	0	Spreading	2	Receives cereal
3	6	14-12/16	Good	......	1¼ × 1¼	+	0	Slight	0	0	Sits	0	+	0	Good	0	Rickets	2	
4	4	12	Good	......	1½ × 1½	0	0	Slight	+	0	0	0	+	++	Soft	0	Rickets	1	
5	9	12- 8/16	Pale	Square	1½ × 1¼	0	0	+	0	+	0	0	+	0	Fair	0	Rickets	2	
6	4½	12	Good	......	¾ × 1	0	0	Slight	0	0	0	0	0	0	Good	0	Negative	2	
7	10	15- 8/16	Fair	......	¾ × ¾	0	0	+	+	+	0	+	++	+	Poor	4 cm.	Negative	3 and radius	Had measles; indoor 3 months; receives cereal and broth
8	6	18- 8/16	Good	......	1¼ × 1	0	0	0	0	0	Sits	0	+	0	Good	0	Negative		
9	8	16-12/16	Poor	......	½ × ½	0	0	+	0	0	Sits	0	++	+++	Poor	0	Spreading	2	
10	6	19	Good	......	1½ × 1	0	0	Slight	0	0	0	0	+	0	Fair	2.5 cm.	Rickets	3	Outdoors once a week
11	8	15	Fair	......	2 × 2	+±	0	+±	+±	+	0	+	++	+	Poor	0	Rickets marked	1	Outdoors once a week; receives milk with zwiebach
12	5	18	Fair	......	1½ × 1¼	+	0	Slight	0	0	0	0	+	0	Soft	0	Rickets	2	Outdoors every day
13	6	15- 8/16	Good	......	1 × 1	0	0	Slight	0	0	Sits	..	++	0	Soft	2.5 cm.	Spreading	2	Never outdoors
14	9	20 8/16	Good	......	1½ × 1	0	0	0	0	+	Sits	+	++	0	Soft	4.0 cm.	Negative	2	
15	6	17- 7/16	Good	......	1½ × 1	0	0	Slight	0	0	0	0	++	++	Poor	0	Negative	2	
16	4	15- 6/16	Good	......	¾ × ¾	0	0	0	0	0	0	0	+	0	Good	0	Rickets (?)	2	Never outdoors
17	4	10-14/16	Fair	......	1 × 1¼	+	0	0	0	0	0	0	++	+	Poor	4.0 cm.	Negative	2	
18	5½	16	Good	......	1½ × 1½	+	0	+	0	+	0	0	++	0	Fair	0	Rickets	2	Out every day
19	4	11-11/16	Fair	......	2 × 2	0	0	0	0	0	0	0	++	0	Good	0	Negative	0	Out every day
20	5	16- 4/16	Good	......	1¼ × 1	0	0	0	0	0	0	..	+	0	Good	0	Negative	0	Out every day
21	9	17- 7/16	Fair	......	1½ × ¾	0	2	+	0	0	Sits	..	+	0	Good	0	Negative	2 and radius	Out every day; receives cereal
22	6½	16 11/16	Good	......	1½ × 1½	0	0	0	+	+	0	..	++	0	Fair	0	Negative	2	Out every day; receives cereal
23	5	16	Good	......	2 × 2	+	0	+	+	0	0	..	++	0	Good	0	Rickets moderate	2	Out once a week
24	7	16- 9/16	Good	......	1 × ¾	0	0	+	0	0	0	..	++	0	Good	0	Rickets	2 and 1	Out every day
25	4	16	Good	......	1½ × 1½	0	0	0	0	0	0	0	++	0	Fair	2.0 cm.	Negative	2	Out every day
	Total	....	....	....	....	7 +	..	9 +	5 +	..	..	..	..	..	...	...	10 rickets		

able expense, we attempted to prevent rickets by means of feeding a large number of babies on certified raw milk. In spite of this excellent diet they developed evidences of mild rickets in the course of the winter. Of the entire group of fifty-three infants, only two were entirely free from signs of this disorder; if we do not accept low inorganic phosphate as equivalent to rickets, seven additional cases must be considered as negative, making nine in all. In our opinion certainly all of these seven cases should not be excluded, as a diminution of inorganic phosphate generally is associated with rickets. It should be borne in mind that these figures do not apply to one month of the winter but to the entire period ending in April. The incidence of rickets increases steadily month by month throughout the winter, being far greater in March than in January, the decrease beginning toward the end of April (in the temperate zone), depending somewhat on local climatic conditions and especially on the character of the season.[10] If these fifty-three cases are judged by the classic text book description of rickets, only nineteen fall into this category. This indicates how difficult it is to state the frequency of rickets, and how its incidence will appear to be high when intensive examinations are employed. These newer diagnostic methods enabled us, however, to begin treatment at the earliest moment, so that many cases were cured in January or February by means of cod liver oil or heliotherapy, which would not have been recognized under ordinary circumstances until some months later when they had become more evident.

CONCLUSIONS

With our broader conception of rickets, diagnosis has become increasingly difficult. Of the immediate clinical signs the most reliable is beading of the ribs, to which more attention should be paid. The great disadvantage of this sign is that it does not aid in differentiating between the active and the inactive phases of the disorder.

Roentgen ray examination of the epiphyses has proved disappointing. Frequently it does not demonstrate lesions at a time when the diagnosis can be established definitely by other methods. A negative roentgenogram has, therefore, little value in deciding the question of early rickets. It is a most valuable sign, however, in judging whether rickets is healing or whether a therapeutic agent is of value.

The inorganic phosphate of the blood is generally diminished in rickets in the early stages, long before the roentgen ray gives evidence of the disorder, and frequently as early as, or earlier than, beading of the ribs. It is not, however, pathognomonic, as there are other factors leading to a diminution of inorganic phosphate. On the other hand, rickets is occasionally met with where the blood analysis is normal in this respect.

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[10] The winter of 1920-1921 was particularly mild, and rickets was correspondingly mild and began to disappear early; the previous winter was exceptionally severe leading to marked rickets and a prolongation of its season.

A group of well nourished breast-fed infants, examined clinically and by roentgen ray at the end of March, showed rickets in more than 50 per cent. of the cases.

Rickets is not only more prevalent in the winter but its incidence increases month by month until April. It is far more frequent in March and April than in December and January. If its incidence is studied when it is at its flood, and use is made not only of the ordinary clinical signs, but also of the newer methods of diagnosis (roentgen ray and chemical tests) we shall find that almost all bottle-fed infants give some indication of rickets.

THE FAILURE OF YEAST THERAPY IN THE FEEDING OF INFANTS *

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Because yeast can be substituted successfully for part of the protein requirements of an adult,[1] is nontoxic,[2] will apparanently improve skin diseases in adults,[3] cure polyneuritis in pigeons,[4] and cause rats on an inadequate diet to gain in weight,[5] numerous advertisements in the non-medical press have acclaimed that yeast in various forms is a panacea for the ills of man and that even infants would be improved by a tablet or two a day. That this conclusion is falsely derived from inapplicable premises is proven not only by the elementary rules of logic, but, furthermore, experiments [6] have shown that when applied to infants, yeast therapy is not only without benefit but may actually do harm. The evidence reported here merely confirms these latter publications.

Demonstrations of the value of vitamin therapy in the feeding of normal infants are not convincing [7] for the majority of them will gain on a dietary regimen alone. If yeast has any real value in causing an infant to gain in weight, it should be fed to patients convalescent from acute intestinal indigestion or to infants suffering from nutritional

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* From the Department of Pediatrics of the Johns Hopkins University and the Harriet Lane Home of the Johns Hopkins Hospital.

[1] Funk, C.; Lyle, W. G.; McCaskey, D.; Caspe, J., and Poklop, J.: The Nutrition Value of Yeast, Polished Rice and White Bread, as Determined by Experiments on Man, J. Biol. Chem. **27**:173, 1916. Hawk, P. B.; Smith, C. A., and Holder, R. C.: Bakers' Yeast as Food for Man, Am. J. Physiol. **48**:199, 1919.

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[7] Matheu, C. P.: Clinical Research on Vitamins, Rev. d. l. Assn. med. Argentina **34**:286, 1921.

disturbances such as chronic intestinal indigestion (celiac disease) or to physically retarded children. The weight of these patients may remain practically stationary for weeks, and, therefore, the value of any therapeutic measures can be tested conclusively. Yeast in total amounts of one-quarter or one-half of a yeast cake per day was added to the diets of nine infants for periods of from eight to twenty-three days. One cake of fresh Fleishmann's yeast was emulsified in 2 ounces of sterile water and from 1 to 3 teaspoonfuls of the suspension (from 1/16 to 3/16 of a cake) was added to each of the infant's milk feedings just before they were offered to the child. Inasmuch as abdominal distension occurred in some of these patients, and their stools became more frequent, and as heating yeast to 105 C does not destroy its growth promoting properties for rats,[5] the emulsions of yeast were made in boiling water after the first week of the experiment. Yeast suspended in boiling water did not produce as marked distension and diarrhoea as the unheated preparation.

REPORT OF CASES

CASE 1 (25989).—W. M., white, male, aged 2 months, admitted to Harriet Lane Home Aug. 27, 1920. Diagnosis: Acute intestinal indigestion.

Family History.—Negative.

Past History.—Negative.

Present Illness.—Onset Aug. 11, 1920, with diarrhea and vomiting. Weight, 7 pounds 10 ounces.

Treatment.—Given protein milk, woman's milk, buttermilk and finally whole milk and sugar formula and farina in amounts of from 94 to 117 calories per kilogram of body weight. Diarrhea and vomiting ceased soon after admission, and weight gradually increased to 10 pounds when discharged Dec. 15, 1920.

Was given one-quarter of a yeast cake daily from Oct. 13, 1920, to Nov. 5, 1920 (twenty-three days). Diet remained unchanged. During this period the weight did not increase more rapidly than before and after yeast therapy (Chart 1).

CASE 2 (246265).—E. G., white, female, aged 5 months, admitted to Harriet Lane Home May 25, 1920; weight, 7 pounds. Diagnosis: Acute intestinal indigestion.

Family History.—Negative.

Past History.—Negative, except for nutritional disturbances.

Present Illness.—Onset March 7, 1920, with diarrhea and vomiting.

Treatment.—Given protein milk, woman's milk, buttermilk and finally whole milk and barley water formula, and farina in amounts of from 95 to 130 calories per kilogram of body weight. Diarrhea and vomiting ceased soon after admission and weight gradually increased to 14 pounds 11 ounces when discharged June 29, 1921.

The infant was given one-quarter of a yeast cake daily from Oct. 13, 1920, to Oct. 19, 1920, and then one-half of a yeast cake daily until Nov. 4, 1920 (twenty-two days). The diet remained unchanged, except for the addition of farina on the last day. Weight remained stationary during most of this period. The patient developed diarrhea, vomiting and slight fever (100 F.) during the last day of this period. She had had several similar upsets prior to yeast therapy (chart 1).

Case 3 (25464).—E. D., white, female, aged 10 months, admitted to Harriet Lane Home Aug. 17, 1920; weight, 11 pounds. Diagnosis: Acute intestinal indigestion.

Family History.—Negative.

Past History.—Negative, except for nutritional disturbances.

Present Illness.—Onset June 18, 1920, with diarrhea and vomiting.

Treatment.—Given protein milk, buttermilk, junket and finally whole milk and barley water formula and farina in amounts of from 83 to 120 calories per kilogram of body weight. Diarrhea and vomiting ceased soon after admission and weight gradually increased to 12 pounds 12 ounces when discharged Dec. 18, 1920.

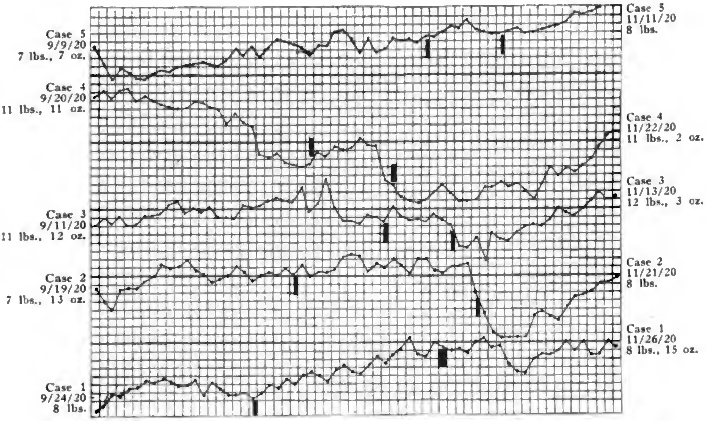

Fig. 1.—Weight curves of five patients convalescent from acute intestinal indigestion to whose diets was added from ¼ to ½ yeast cake daily for from eight to twenty-three days (spaces between blocks). Each space on ordinates represents 2 ounces; on abscissae one day.

Was given one-quarter of a yeast cake daily from Oct. 16, 1920, to Oct. 24, 1920 (eight days). Diet remained unchanged. Weight remained practically stationary during this period (Chart 1).

Case 4 (23,773).—M. D., white, female, aged 7 months, admitted to Harriet Lane Home Aug. 27, 1920; weight, 13 pounds 2 ounces. Diagnosis: Acute intestinal indigestion.

Family History.—Negative.

Past History.—Negative, except for nutritional disturbances.

Present Illness.—Onset Aug. 14, 1920, with diarrhea and vomiting.

Treatment.—Given protein milk, buttermilk and finally whole milk and water formula and farina in amounts of from 70 to 116 calories per kilogram of body weight. Diarrhea and vomiting ceased soon after admission and weight after falling to 10 pounds 2 ounces gradually increased to 13 pounds 3 ounces when discharged Jan. 9, 1921.

Was given one-quarter of a yeast cake daily from Oct. 16, 1920, to Oct. 26, 1920 (ten days). Diet remained unchanged. Weight increased slightly at first, but the patient became very distended during this period. In the last two days of yeast therapy, diarrhea and refusal of food developed. She had had several similar upsets prior to yeast therapy (Chart 1).

Case 5 (26097).—W. T., white, male, aged 6 months, admitted to Harriet Lane Home Sept. 7, 1920; weight, 7 pounds 6 ounces. Diagnosis: Acute intestinal indigestion.

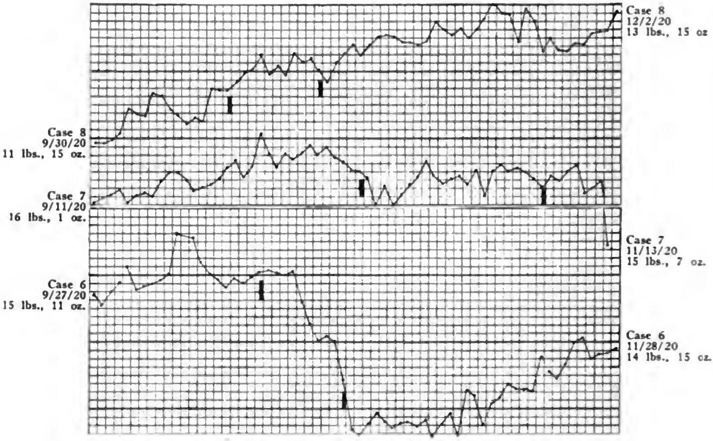

Fig. 2.—Weight curves of three patients with chronic intestinal indigestion to whose diet was added ¼ yeast cake daily for from ten to twenty-two days (spaces between blocks). Each space on ordinates represents 2 ounces, on abscissae one day.

Family History.—Negative.

Past History.—Negative, except for nutritional disturbances.

Present Illness.—Onset Aug. 1, 1920, with diarrhea.

Treatment.—Given protein milk, woman's milk, buttermilk and finally whole milk and barley water formula and farina in amounts of from 86 to 125 calories per kilogram of body weight. Diarrhea ceased soon after admission and weight gradually increased to 9 pounds 10 ounces when discharged Jan. 1, 1921.

Was given one-quarter of a yeast cake daily from Oct. 19, 1920, to Oct. 28, 1920 (nine days). Diet remained unchanged. During this period the patient's weight did not increase more rapidly than before and after yeast therapy (Chart 1).

Case 6 (23907).—K. W., white, male, aged 21½ months, admitted to Harriet Lane Home Feb. 9, 1920; weight, 14 pounds 6¼ ounces. Diagnosis: Chronic intestinal indigestion.

Family History.—Negative.

Past History.—Negative.

Present Illness. — Onset August, 1919, with vomiting, progressive loss of weight and slight diarrhea.

Treatment.—Given protein milk, woman's milk, buttermilk, junket, farina, eggs, meat and vegetables in amounts of from 80 to 107 calories per kilogram of body weight. The symptoms ceased soon after admission, and the weight, with the exception of six digestive upsets, gradually increased to 23 pounds 8 ounces when discharged March 26, 1922.

Was given one-quarter of a yeast cake daily from Oct. 16, 1920, to Oct. 26, 1920 (ten days). Diet remained unchanged. The patient's distension became more marked, and after four days of yeast therapy, a digestive upset occurred with diarrhea, rapid loss of weight and slight fever (100 F.). The patient had had similar digestive disturbances previously (Chart 2).

Case 7 (25261).—T. E., white, male, aged 2 years. Admitted to Harriet Lane Home July 2, 1920; weight, 16 pounds 2 ounces. Diagnosis: Chronic intestinal indigestion.

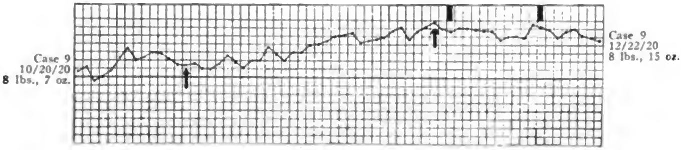

Fig. 3.—Weight chart of mentally and physically retarded patient, to whose diet was added ¼ yeast cake daily for eleven days (spaces between blocks) and later from ½ to 1 ounce of fresh veal liver daily for thirty days (spaces between arrows). Each space on ordinates represents 2 ounces, on abscissae one day.

Family History.—Negative.

Past History.—Negative.

Present Illness.—Onset June, 1919, with loss of appetite, distension and progressive loss of weight.

Treatment.—Given protein milk, buttermilk, junket, farina, eggs and meat in amounts of 80 to 97 calories per kilogram of body weight. Symptoms improved soon after admission but the weight remained practically stationary and then fell to 15 pounds 7 ounces when discharged Nov. 13, 1920.

Was given one-quarter of a yeast cake daily from Oct. 13, 1920, to Nov. 4, 1920 (twenty-two days). Diet remained unchanged. During this period the weight did not increase more rapidly than before and after yeast therapy (Chart 2).

Case 8 (20766).—A. B., white, female, aged 22 months. Admitted to Harriet Lane Home Sept. 13, 1920; weight, 11 pounds 2 ounces. Diagnosis: Chronic intestinal indigestion.

Family History.—Negative.

Past History.—Negative.

Present Illness.—Onset July, 1920, with diarrhea and progressive loss of weight.

Treatment.—Given protein milk, woman's milk, buttermilk, junket and meat in amounts of from 90 to 111 calories per kilogram of body weight. Diarrhea ceased soon after admission and weight gradually increased to 16 pounds 7¼ ounces when discharged, June 28, 1921.

Was given one-quarter of a yeast cake daily from Oct. 16, 1920, to Oct. 27, 1920 (eleven days). Diet remained unchanged. During this period the weight did not increase more rapidly than before and after yeast therapy. The patient became moderately distended (Chart 1).

Case 9 (24913).—E. S., white, female, aged 11 months. Admitted to Harriet Lane Home May 19, 1920; weight, 11 pounds 2 ounces. Diagnosis: Mental and physical retardation of development.

Family History.—Negative.

Past History.—Premature (7 months); birth weight, 2 pounds 4 ounces; otherwise negative.

Present Illness.—Failure to gain in weight.

Treatment.—Given whole milk, barley water and sugar formula, buttermilk, farina, maltsoup and broth in amounts of from 8 to 164 calories per kilogram of body weight. Weight increased very slowly to 13 pounds when discharged, June 9, 1921.

Was given one-quarter of a yeast cake daily from Oct. 27, 1920, to Nov. 7, 1920 (eleven days). Diet remained unchanged. The weight remained stationary.

As fresh veal liver is reported to be rich in vitamins A and B,[5] ½ ounce of this was given daily from Nov. 9, 1920, to Nov. 25, 1920. The amount of veal liver was then increased to 1 ounce daily and continued until Dec. 9, 1920 (a total of thirty days). Diet otherwise remained unchanged. The gain in weight during this period was no greater than in other periods without veal liver therapy (Chart 3).

SUMMARY

1. *Acute Intestinal Indigestion.*—These six patients (Chart 1) had recovered from the acute diarrheal stage of the condition, and their weight and "tolerance" for food were slowly but gradually increasing. The weights of these six infants did not increase more rapidly during the period of yeast therapy than prior to the experiment. No improvement in their general condition could be noted. In fact, two patients during the period of yeast feeding developed diarrhea and rapid loss of weight. However, these infants had had similar upsets previously so that the yeast may not have been altogether responsible for these relapses.

2. *Chronic Intestinal Indigestion.*—These three patients (chart 2) were in no way benefited by yeast therapy. They all became distended; their weight showed no increase that could be attributed to yeast, and one infant had a severe relapse of diarrhea and loss of weight. Yeast, however, may not have been responsible for this last result for the patient had had similar attacks prior to yeast therapy.

3. *Physical Retardation.*—This patient (Chart 3) although without demonstrable intestinal disease, had failed to gain in weight, in spite of being fed an apparently adequate diet. Yeast therapy, or even feeding fresh veal liver, which is rich in vitamins,[5] had no effect, either beneficial or harmful, in this instance.

CONCLUSION

As far as may be judged from this very limited series of cases, the administration of yeast to patients convalescent from acute intestinal indigestion, to infants suffering from chronic intestinal indigestion and to a physically retarded child is without benefit and may possibly be harmful.

RABBIT HAIR ASTHMA IN CHILDREN *

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Walker has notably added to our better understanding of asthma by giving an extensive working foundation. Many other workers have since contributed large series of studied cases. They all, however, report a certain number of cases in which the causative agents could not be found. Walker,[1] for example, found 50 per cent. which did not react to any proteins. In the most recent classification by Rackemann,[2] 41 per cent. of the true asthmatics did not react to proteins. Naturally, in work of this kind there are many factors which make it difficult to study cases completely, and were it possible for investigators to do so more exhaustively, the unclassified group would undoubtedly be smaller. Our series of cases offers an example of just such a group which would have remained unclassified had it not been our good fortune to discover the offending protein in the first case which suggested the search for the others. In this way workers are continuously drawing attention to new substances—and it might be better therefore to always consider an unclassified case as one temporarily undiagnosed, the causative agent of which may some day be found.

Historical.—Blackley,[3] in 1873, reports the first case in the literature of a man, aged 54, who since the age of 17 showed symptoms of asthma whenever in the presence of rabbits. Recently Freeman[4] reported a case of "a man who has always hated the presence of rabbits, or rabbit meat or rabbit skin. He is devoted to shooting but always has to get the keepers to put him where there have not been rabbits about, otherwise he knows he will not hit a bird." Sporadic cases are cited of laboratory workers who get attacks of asthma when working with rabbits, and persons whose attacks are precipitated by contact with pets. In all these cases it has been direct contact with the animal which has brought about the reaction. Several writers have obtained positive reactions to rabbit hair in their routine skin tests, but make no mention of the source. One of these is deBesche,[5] who

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1. Walker, I. C.: Bronchial Asthma, Oxford Loose Leaf Medicine.

2. Rackemann, F. M.: Clinical Classification of Asthma Based on a Review of 648 Cases, Am. J. M. Sc. **162**:802 (Dec.) 1921.

3. Blackley, C. H.: Hay Fever, London, 1880, Ed. 2.

4. Freeman, J.: Toxic Idiopathies, Lancet **2**:229 (July 31) 1920.

5. DeBesche, A.: Hypersensitiveness and Asthma, Especially in Relation to Emanations from Horses, J. Infect. Dis. **22**:594, 1918.

in his interesting paper on horse asthma mentions the cases of two persons who also reacted to rabbit hair. He refers to another patient whose asthmatic attacks were precipitated by the material in the mattress and pillow which contained a mixture of horse, cow, cat hair and wool, the removal of which cured the patient. Vander Veer,[6] however, cites the only case which we have been able to find in the literature of asthma which was caused by rabbit hair found in the pillows on which the patient slept. He states that this is an extreme case, but from our experience it does not appear to be so rare.

CASE REPORTS [7]

CASE 1.—J. R., boy, 5½ years of age, was referred to our clinic more than a year and a half ago suffering from asthma. His family history was absolutely negative for any form of protein sensitization. The child had been perfectly well up to 6 months of age; from that time on he suffered from repeated attacks of coryza, and at the age of 1 year (after the family moved to Coney Island) he developed his first attack of asthma. He continued to have these attacks, and during the year prior to admission they had become more frequent and more severe. They were invariably preceded by running nose, sneezing, watery eyes and cough. These prodromata would last for about a day, and at night his asthmatic attack would precipitate, with a gradual subsidence after two to three days. Vomiting and loss of appetite attended all attacks.

The mother insisted that something in Coney Island caused these attacks because the child had never suffered from asthma before they moved there, and whenever she visited with him in Albany or Hudson he was free from attacks. The child was tested repeatedly with all the proteins we had on hand—food, bacterial, and animal (rabbit hair was not one of the stock proteins at that time), and they were all negative. The child continued to have his attacks, however, and they became more frequent and more severe. But we could do nothing further and this case had to be classified as unsolved.

Several months later the child in one of his severe attacks was advised admission into the hospital and made a very rapid recovery. On the night of his return to his home he promptly developed another severe attack which lasted for three days. A week later I was hurriedly summoned to the child—this was my first home visit. I found the child at the height of a most intense attack. I noted on the blanket covering the child a great many small fine hairs. I ordered the child to another room, and opened all the pillows, the mattress and comforter. They all contained what appeared to be rabbit hair. Here I felt that we had probably discovered the cause of the child's asthma. I ordered the pillows, etc., to be removed, and the house thoroughly cleaned.

Several days later the boy was tested and he gave positive reactions to the cutaneous test with the hairs removed from the pillows, and with the protein extract prepared by the Arlington Chemical Company. To further prove to the mother that the child was sensitive to rabbit hair, the child was taken to the laboratory and was given a rabbit to play with. After five minutes he began to complain that the room was getting very close, to rub his nose, and then to sneeze. I asked him to play with the rabbit more vigorously, to run after it and pull its fur. He sneezed again, rubbed his nose, and his eyes became watery. His breathing by now was extremely heavy and he felt very sick. This state became progressively worse, and in a few minutes he developed a typical severe attack of asthma. The entire sclera of the right eye became congested, the conjunctiva and eyelid markedly edematous, giving a beautiful picture of angioneurotic edema. On examination a rabbit hair was found in the eye. A hypodermic injection of epinephrin promptly relieved the asthma and eye condition, but the asthma recurred that night in a mild form.

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[6] Vander Veer, A. J.: The Asthma Problem, New York M. J. **112**:392, 1920.

[7] Ratner, B.: M. Clinics N. America **5**:1129 (Jan.) 1922.

This child has been under my observation continuously and has been free from attacks, except once or twice when we have been able to trace them to attempts at desensitization or contact with bedding containing the rabbit hair—and once when playing with a toy made of rabbit hair.

This case was so impressive that we immediately sent word to three other patients who repeatedly gave negative reactions to the various proteins. All were positive to rabbit hair.

Case 2.—S. G., boy, aged 9½ years. Family history absolutely negative for protein sensitization. Since his early infancy, the mother states, the child had attacks of what might have been asthma, and as far back as she can remember he has always suffered from coryza and recurrent bronchitis. Mother dates his first real attack at about 1 year of age. Asthma has been repeatedly diagnosed at different hospitals since then.

Attacks usually start with a dry cough and almost invariably precipitate between 12 midnight and 1 a. m.; they generally last for two or three days, during which time the child would vomit his food and feel generally sick. They occur perennially once every week or two. They have, however, become less frequent, now occurring every five or six weeks.

The mother attributed his attacks to eating candy and running around on the street, coming into the house all tired out. However, after going through the gamut of our proteins, we could not locate the source of his trouble. We tested this boy with rabbit hair and were rewarded with a positive reaction.

I then questioned the mother about her pillows. She was quite certain that they were filled with goose feathers, and stated that the child had slept on them from birth. But the following day she returned with a bag full of rabbit hair obtained from the pillows. I took some of this hair, had the child breathe it in, and rubbed some into his nose. While he did scratch his nose and sneeze, no asthmatic attack ensued. A little disappointed I took the boy to the animal house. The child held the rabbit in his arms and shook the fur. In a few minutes his eyes became watery, nose itchy, with a slight mucus discharge. By now asthmatic wheezes were heard in the chest, but no attack developed. However, I told the mother to be sure to discard the pillows that night. The next day the mother telephoned to advise me that the child had had an extremely severe attack following his return from the hospital.

This boy is still under my observation and is free from attacks—with the exception of several attacks which were caused by injections or exposure to rabbits.

Case 3.—M. R., boy, aged 7 years. Family history is negative for asthma, etc. For the first two years of his life the child was perfectly well. At the age of 2 the family moved from Brooklyn to Providence, where they lived at the home of the grandmother. On his arrival he contracted a cold, developed diphtheria, and two weeks later pneumonia. He was in the hospital three weeks, dangerously ill. However, he recovered, and was brought home in a very weakened condition. A week after his return from the hospital he developed his first attack of asthma.

He then moved to New Bedford to live with his mother's sister, where he had repeated attacks occurring every two weeks. They were always preceded by sneezing, coughing, and suffusion of the eyes; asthma would then set in and last for three days. The child always complained of pains in the stomach region and would vomit a great deal. The mother then lived with another sister in Providence for several months and there the child was free from attacks.

On his return to New York the attacks recurred and continued. As in the other two cases, all tests reacted negatively until we tried the rabbit hair.

The home was carefully investigated, but no trace of rabbit hair was found in pillows or other bedding. In this case it was the father who was at fault. He was employed in a men's hat factory, and his duties were to rub down the rough felt with pumice. Investigation revealed a tremendous amount of finely broken up hairs on his clothing and person. A letter from a Danbury hat factory stated that rabbit fur was used in the manufacture of practically all felt hats. Dust from the factory was extracted and gave a positive skin reaction in this case and all the other cases of rabbit hair hypersensitiveness.

This child, too, was given a rabbit to play with, but developed no reaction until four hours later. It is interesting here to note that this child gave the greatest skin reaction of any of the cases, and showed the slowest clinical response. The attack lasted for two whole days and adrenalin injections gave only temporary relief.

The mother visited the homes in Providence and New Bedford, and returned with rabbit's hair from the pillows. The pillows in the home of the sister where he had been free from attacks, however, contained goose feathers.

The father has been advised to take the greatest precaution to remove all the factory dust after the day's work. The child still continues, however, to have occasional attacks which are probably due to the fact that the father cannot free himself entirely from this dust.

Case 4.—I. M., boy, 7½ years old at the time of admission. The same situation prevailed as in the former cases. The mother dates the first attack of asthma from 8 months of age; and from earliest infancy the child has had coryza and bronchitis. He has practically never been free from attacks, and the intervening times between attacks he always suffered from chronic coryza. His attacks also lasted from two to three days and the child also vomits during attacks and suffers loss of appetite. The search for rabbit hair was very discouraging, but the offending pillow was finally located. He had used this since birth. When it was opened much of the contents floated into the room and the child developed an attack of asthma. A clinical test with a live rabbit resulted similarly to the other cases, but this child, in addition, developed large urticarial wheals wherever the hairs rubbed against the face or body. This child has improved tremendously since removal of the pillows but has suffered several attacks in the past year which were directly traced to rabbit hair at a neighbor's home.

Case 5.—H. G. During our studies the two brothers of Case 2 always came to the clinic. One day when all the asthmatics were playing vigorously with the rabbits, these two children (aged 6 and 3, respectively), also joined in the sport. After I had examined my patients I was attracted to the 6 year old, who had suffused eyes, running nose and rapid breathing. Examination disclosed definite asthmatic wheezes. I immediately tested him with rabbit hair and obtained a positive skin test. The mother then recalled that three years before, after he had undergone a mastoid operation and a rather severe pneumonia, he had what she now thinks might have been asthma, though she never thought further of it. This child, it will be noted, also slept on the pillow, but inasmuch as it had been removed—for a year and a half now—has shown no further attacks.

Case 6.—M. S., a boy, 9 years of age, came to the clinic a year and a half ago, before the aforementioned cases had come to my notice. The child at that time reacted to lactalbumin and beef. After our initial studies this boy failed to return. During the period of absence the child suffered continuously from asthma, the attacks coming on usually at night. Before taking any further steps at this visit I requested the mother to bring me samples of the pillows and other bedding. Three of the pillows contained rabbit hair. A cutaneous test was made with these hairs and the regular rabbit hair protein and in both cases positive reactions were obtained. It might be interesting to note that the child had asthma for the past six years and the pillows had been in the possession of the family six and one half years.

Case 7.—G. H., a girl, aged 5. Father a hay-fever sufferer. Last winter the child suffered from colds and recurrent bronchitis. This year still suffered from coryza, but to a much less extent. I was attracted to the child's hat, which was made of rabbit fur. I noted that the hairs flew off easily. On further questioning I was informed that last year the child had worn an entire coat made of the same fur. The mother noted that the hairs were easily shed, and therefore discarded the coat this winter. A cutaneous test for rabbit hair revealed a positive reaction, and I advised discarding the fur hat.

Case 8.—M. M., 20 months old, since infancy has suffered from coryza and recurrent bronchitis; has had about six attacks of asthma this past year; gave a positive skin test to rabbit hair. A visit to the home revealed a large pillow filled with the hair which was used only occasionally. On questioning the parents, the father recalled that the previous summer when the child played with a rabbit he got a severe attack of asthma. This occurred in the country and the family immediately returned to the city. No importance was attributed to this at that time. The fact that the pillow was used only occasionally accounts for the infrequency of the attacks. I might bring out a further interesting fact: this pillow was given the family by an aunt who has since died of tuberculosis and who had always suffered from asthma.

DISCUSSION

Distribution of rabbit hair.—Rabbit hair as an etiologic factor at first hand seems of little practical significance, but strangely enough this particular hair was disclosed to have a very wide distribution. The soft downy fur immediately next to the rabbit skin is used in the manufacture of practically all felt hats, and therefore the rabbit hair which covers this fine fur is discarded and sent broadcast to be used in the various manners so nicely brought out in the above cases. Insofar as it is used in pillows, comforters, mattresses, as furs, and children's clothing, toys, and is found in felt hat factory dust, and because the animal itself is used in laboratories and as pets, rabbit hair as a potential factor in the production of asthma should be placed in the first rank, along with horse hair, goose and chicken feathers.

Attempts at desensitization with some interesting reactions and observations.—An attempt was made to desensitize the first four cases by repeated gradually increasing doses of the rabbit hair extract. We have utterly failed to accomplish our purpose and have only succeeded in leaving the patients as sensitive as they were before. However, the failure may partly be due to the fact that we chose the rapid method of desensitization. I will not go into a detailed report of the many months these cases were worked with but will indicate some findings and conclusions we arrived at.

Itching at the point of injection seems to indicate that we should go to a higher dilution, that we are approaching the threshold. Any local reaction, particularly one that persists for quite a time, indicates that we are above the threshold of tolerance, and that we should go back to a much weaker dilution.

Biologically every case varies and we should be prepared for any exigency which may occur, by always having epinephrin at hand. This was illustrated by Case 2. We thought the child was becoming rapidly desensitized, and of all the cases showed the least reactions. When we were giving a rather large dose, 0.4 c.c. 1 :500, to him—using exactly the same dose, the same material and the same syringe with Case 4—the child in a few minutes began to show signs of acute reaction, marked scratching, dyspnea, pain in the chest, and moderate cyanosis. The child vomited and then became markedly asthmatic. Fifteen minims of epinephrin were immediately given and after being observed for two hours, the symptoms gradually subsided. He was then sent home, and that night developed marked urticaria and for the next few days was extremely sick, still suffering from asthma. The child in Case 4 took the injection without any trouble—although he had apparently been the more sensitive of the two.

With Case 3, after showing local reactions of small wheals and indurations to the first three injections, which were very small 0.05, 1 : 100,000, when the fourth dose was given, 0.08, the child developed a large urticarial wheal which became larger and larger until it gradually involved the whole forearm. That night he developed a severe attack of asthma which lasted for six days. With every case we had asthmatic attacks as a direct result of overstepping the warning of local reactions.

After these various accidents occurred we returned to much weaker dilutions and injected at weekly intervals. But after this had received a thorough trial the patients were found to be just as sensitive. Further studies will be made with new cases and from our experience we would strongly urge that one always work with much weaker dilutions than shown by the skin tests and regard all local reactions as impending danger and therefore go slowly.

Rackemann[8] discusses two interesting reactions during treatment with horse hair extract which are the exact prototypes of Cases 2 and 3. In the first case, which developed severe symptoms, he struck a vein. His conclusions, which agree with mine, are: "The acute shock illustrates well the danger which always exists in the treatment of these cases regardless of the size of dose or care of administration. The typical serum disease with all its clinical manifestations illustrates another danger and furthermore suggests a possible accumulation of antigenic substance in the cells with explosive manifestations when this accumulation has reached a certain point." A further explanation for our acute reactions may be found in the recent work of Lewis,[9] who concludes that absorption of serum from the subcutaneous tissues is very slow and the main route of absorption from the subcutaneous tissue is through the lymphatics; and because of the suddenness with which acute symptoms appear he feels that the instances of acute death in man following subcutaneous injections are due to an accidental intravenous injection. The need of care to exclude as far as possible the injury to a subcutaneous blood vessel during subcutaneous injection is indicated.

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[8] Rackemann, F. M.: Interesting Reactions Obtained During Treatment of Two Cases of Bronchial Asthma, J. A. M. A. **69**:889 (Sept. 15) 1917.

[9] Lewis, J. H.: Route and Rate of Absorption of Subcutaneously Injected Serum in Relation to Occurrence of Sudden Death After Injection of Antitoxic Horse Serum, J. A. M. A. **76**:1342 (May 14) 1921.

Dosage and Temporary Desensitization.—The question has always arisen in our minds why Case 2 almost invariably got his attacks about twelve, midnight. Was it because going to bed at 8:00 p. m. it took about four hours before he inhaled a sufficient amount of the hair to produce his attack? In Case 3 asthma did not develop until four hours after playing with the rabbit. Another patient, who previously had reacted as the others did, several months later was told to stand at the farther end of the laboratory while the other boys played vigorously with the rabbit. All the others developed asthma, and he alone only showed symptoms of suffusion of the eyes and sneezing which passed off readily. Another boy had no asthma while we were hunting for the offending pillow at his home, but when the pillow was opened, the hair floating into the small room, with the boy near by, brought on an attack. One has but to see a beam of sunshine striking a dust filled room to realize what a tremendous dosage can thus float in the air. These instances all indicate the importance of dosage.

If these children are refractory between the attacks, for weeks at a time, the explanation might be one of small dosage, but more likely one of desensitization. For example, Case 2, who developed a severe reaction after a large injection, did show this refractiveness when brought in contact with the rabbit six days later, for he had absolutely no asthma after vigorous playing; but several weeks later, when similarly exposed, an attack of asthma did ensue. This case was the only one who lost his skin sensitivity during this apparently insensitive period. This loss of skin reactivity has been brought out by Schloss[10] in his article on allergy.

Are These Cases Acquired or Hereditary?—Many questions arise in a study of this sort which must of necessity still await absolute scientific proof. A most pertinent question that arises in the mind of every investigator in this field is whether cases of this kind are hereditary or acquired. A great number of cases give a family history of disturbances probably due to allergy. Cooke and Vander Veer,[11] Longcope[12] and

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10. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**: 433 (June) 1920.

11. Cooke, R., and Vander Veer, A.: Human Sensitization, J. Immunol. **1**: 201 (June) 1916.

12. Longcope, W. T.: The Susceptibility of Man to Foreign Proteins, Am. J. M. Sc. **152**:625 (Nov.) 1916.

others favor the hereditary view. Other reports, however, indicate the possibility that the condition may be acquired. Walker[1] cites the case of a woman whose asthma when coming in contact with horses developed after an injection of horse serum. Duke[13] cites another case of an individual who became sensitive to honey after being stung by a bee. Schloss[10] submits strong evidence for acquired sensitization. In thirty-three out of eighty cases Schloss obtained no history of allergic disturbances in the family. Of these thirty-three persons, however, sixteen developed symptoms the first time a particular food was eaten, so that the condition was in all probability congenital, although there was no history indicating that it was inherited. In the remaining seventeen cases, he states, the food in question was eaten some time before the characteristic symptoms appeared. And his conclusion is that the only explanation for this group is that sensitization was acquired.

Histories are to a great extent worthless as evidence of absolute proof for any given viewpoint. However, after a most careful investigation we were unable in our cases to find any history or other evidence which might indicate hereditary acquisition and since in all of our cases prolonged contact with the rabbit hair in early infancy preceded development of the attacks we are inclined to favor the view that the condition, in these cases at least, was an acquired one, as Schloss has found with his series of cases.

Is the Hair Itself the Inciting Substance?—Practically all writers on animal hair sensitization have had their patients affected by direct contact with the animal, and it was difficult to eliminate factors other than the hair. But in our series where all the patients came in contact with the hair in an absolutely dry state, as the pillows, etc., were many years old and the extract of this hair gave positive skin tests there can be little question of the responsibility of the hair itself for the condition. I might add that in two cases a skin reaction was also obtained to the dyed rabbit hair.

Few patients sensitive to animal hair also react to the serum. Rackemann[14] tells of thirty-seven patients who reacted positively to horse hair only five reacted to horse serum as well. Walker[15] out of nine cases found that only one reacted to both horse hair and serum. Of our series only one reacted to rabbit serum.

The lack of correlation between sensitiveness to the hair and similar susceptibility to the serum requires further investigation.

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[13] Duke, W. W.: Food Allergy as a Cause of Abdominal Pain, Arch. Int. Med. **28**:151 (Aug.) 1921.

[14] Rackemann, F. M.: Clinical Study of One Hundred Cases, Arch. Int. Med. **22**:517 (Oct.) 1918.

[15] Walker, I. C.: Study XIV, J. M. Research **31**:423 (July) 1917.

Analysis of Symptoms.—The majority of our patients suffered from chronic coryza and recurrent bronchitis from earliest infancy. Walker,[16] Missildine,[17] Marfan [18] and Mason [19] also find that in infants and children who develop asthma there is practically always a history present of the subjects having had repeated colds and recurrent bronchitis long before their asthma developed.

In analyzing the symptoms of these cases it will be noted that apart from the running nose, sneezing, suffusion of eyes and asthma, virtually all the patients complained of pain in the stomach region and vomiting; that when a hair got into the eye angioneurotic edema and conjunctivitis ensued, and that local contact with the skin caused urticaria. The vomiting might be brought about by nervous reflex stimulation or by swallowing the hair or juices which irritate the stomach mucosa. It is conceivable too that chronic eye conditions like blepheritis or conjunctivitis might come about from continued contact with the hair, and it is common knowledge that animal hair can produce chronic eczema. A classical case was that cited by Markley [20] whose patient had a most severe "anaphylactoid dermatitis" over her head, face, chest, back and hands which was finally traced to a pet guinea-pig which crawled up her arms and shoulders whenever she cleaned his cage. Cure ensued upon the removal of the animal, although she had been refractory to a year's treatment prior to this discovery. In view of the above, vomiting and eczema should not be regarded as foreign to animal hair hypersensitiveness.

CONCLUSIONS

Rabbit hair as an etiologic factor in the production of asthma would at first hand appear to be of little practical significance. But as we have shown its distribution is very wide spread, and it should be placed second to horse hair as a causative agent in the keratin group of asthmas.

While we have not been successful thus far in desensitizing this group of cases the removal of the hair is easily accomplished and avoiding the hair relieves the patients of all symptoms. In attempts at desensitization attention is called to certain dangers inherent in this form of treatment, and adrenalin should always be kept on hand to cope with any exigency which might arise.

Dosage undoubtedly plays a great rôle in the actual production of attacks.

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[16] Walker, I. C.: Bronchial Asthma, Oxford Loose Leaf Medicine.

[17] Missildine, J. G.: Horse Asthma, New York M. J. **100**:825, 1914.

[18] Marfan, A. B.: L'Asthme des nourrissons, Presse méd. **28**:481 (July 17) 1920.

[19] Mason, F. R.: Bronchial Asthma in Childhood, New York M. J. **112**:399 (Sept.) 1920.

[20] Markley, A. J.: Arch. Dermat. & Syph. **2**:722 (Dec.) 1920.

Human beings are capable of showing what might be called temporary desensitization.

Eczema, vomiting, angioneurotic edema, urticaria, conjunctivitis may all occur as a direct result of contact with animal hair, besides the classical symptoms of asthma.

In spite of most careful investigation we were unable in our cases to find any history or other evidence which might indicate hereditary acquisition, and since in all of our cases prolonged contact with the rabbit hair in early infancy preceded development of the attacks we are inclined to favor the view that the condition, in these cases at least, was an acquired one. This differs distinctly from the point of view of Cooke, Vander Veer, Longcope and others.

We would like to suggest that rabbit hair, and all fine dust producing substances, be kept out of pillows, mattresses, clothing and toys, etc., that are used for infants and young children. Infants suffering from chronic coryza and recurrent bronchitis should be carefully studied from the standpoint of their being potential asthmatics.

CLINICAL DEPARTMENT

DIAPHRAGMATIC HERNIA IN A NEW-BORN

REPORT OF A CASE *

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Congenital diaphragmatic hernia, due to weakness or defect of one of the several fibrous portions of the diaphragm, is no longer considered as an extremely rare condition. Occasionally remaining symptomless throughout life, the condition has in several instances furnished a necropsy surprise and its recognition in infancy or later life has most often been due to the occurrence of chronic digestive disturbances or acute obstruction of some portion of the intestine.

In the case reported herewith, the circumstances that the infant was born in the hospital; that it was under observation throughout life; and that it was breast fed and at no time suffered any other illness, accident or disease, make the clinical features manifested as a result of the hernia unusually clean cut.

These are: (1) an acute and alarming respiratory syndrome due to the presence of almost all of the intestine in the left thorax, but with no gastro-intestinal symptoms; (2) subsequent anatomic alteration of the growing infantile thorax and abdomen in response to the altered location of viscera, and (3) the inclusion of the stomach in the hernia, with a high degree of obstruction at the cardia.

Figure 1, a schematic drawing of the diaphragm taken from an article by Keith,[1] who made an anatomic study of the specimens of diaphragmatic hernia in the British Medical Museum, shows the fibrous "weak spots" in the diaphragm, through which hernia of the abdominal contents into the thorax may take place. The number of cases in his series occurring through each of these potential openings is also indicated.

The physical and roentgenologic examinations made it reasonably certain in this case that the hernia took place through the "left pleuroperitoneal passage," i. e., in the most common location.

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* Received for publication May 1, 1922.

* From the Medical Department of Mt. Sinai Hospital.

[1] Keith, A.: Remarks on Diaphragmatic Hernia, Brit. M. J. **2**:1297, 1912.

REPORT OF CASE

H. B., the second child of Russian Jewish parents, was born Nov. 30, 1920, at Mt. Sinai Hospital.

History.—There was no history of hernia or developmental defects among the immediate relatives. He was born at full term, weighed 4,120 gm., cried promptly after birth, had good color, and no abnormalities of any kind were noted. He nursed well, began to gain in weight on the fourth day; had no vomiting, jaundice, or bad stools, and until the eighth day, no cyanosis, pallor, or respiratory difficulty.

On the eighth day the infant had two transitory attacks of slight cyanosis with rapid breathing for which examination revealed no cause, the lungs and heart being found normal, and the heart in the normal left side position. The following morning, shortly after nursing, he suddenly became intensely cyanotic, with rapid, dyspneic respiration, and lay limply in the dorsal position, with an appearance of impending exitus. The cyanosis was somewhat lessened by removing a rather snug abdominal band, and much more by holding the child in a vertical position, but recurred promptly when the child was laid down.

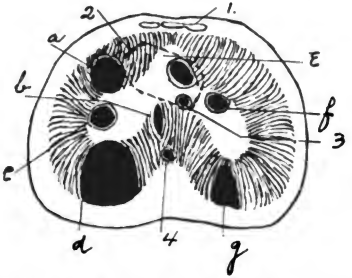

Fig. 1.—Diagram (from Keith) to show the sites of diaphragmatic hernia. Upper, or thoracic, aspect of diaphragm represented. 1, Sternum; 2, pericardium; 3, inferior vena cava; 4, aorta; *a*, sternocostal site, 5 cases; *b*, esophageal orifice, 1 case; *c*, central site, 2 cases; *d*, left pleuroperitoneal passage, 17 cases; *e*, into pericardium, 3 cases; *f*, through right leaflet of diaphragm, 2 cases; *g*, right pleuroperitoneal passage, 4 cases.

Examination.—The respiration rate was from 96 to 100 per minute and in inspiration the upper portion of the anterior thorax was pushed forward and outward, especially on the right, while the lower part of the sternum and inner portion of the costal borders was retracted. There was no movement of the outer portion of either costal border. No cardiac impulse could be seen, but by palpation and auscultation the apex was found to be in the fourth right interspace, 1 cm. inside the nipple line, and percussion outlined a corresponding area of cardiac dulness. Except for this, the right thorax was everywhere hyperresonant, while the left side was tympanitic throughout, the tympany being of the highest pitch and most intense in the axilla. No breath sounds could be heard on auscultation of the left chest, except at the apex, where they were faint but vesicular.

The abdomen was fuller above the umbilicus than below, and without general or local rigidity or tenderness. There was a complete absence of the usual tympany except in the left hypochondrium. A small, smooth, ovoid, mass (kidney? spleen?), freely movable, could be palpated in this region.

Diagnosis. — A diagnosis of left diaphragmatic hernia, due to congenital defect of the diaphragm, was made, and from the absence of vomiting or other gastro-intestinal symptoms it was thought that the stomach was not involved in the hernia and that there was no obstruction. This was confirmed by fluoroscopic and roentgenographic examination after an opaque meal, which showed the stomach to be normal in appearance and position while all of the intestine from the duodenum to the descending colon was above the diaphragm in the left chest and the heart was displaced into the right chest.

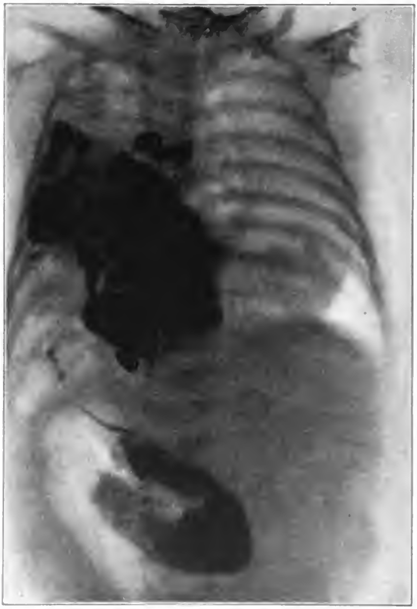

Fig. 2.—Roentgenogram taken one and one-half hours after barium milk feeding.

Treatment.—Since cyanosis and respiratory embarrassment were greatly relieved by holding the infant in a vertical position, it was fastened firmly to a board of proper size by means of bandages, and the board elevated at an angle of more than 45 degrees.

Relief by postural treatment was marked and immediate. The cyanosis promptly disappeared, but for several weeks recurred when the baby was put in a horizontal position. Nursing, stools and sleep were normal, as was also gain in weight, and he was discharged on the fifteenth day, operation at a later time in the nursing period having been advised.

Course.—During the next four months his gain in weight and his general condition were so satisfactory that his parents refused to permit operation. The process of anatomic adjustment to the unusual location of the intestines continued, the anteroposterior diameter of the chest increasing until the child had a veritable barrel chest, while a marked precordial bulging developed in the right thorax. The muscles of the lower abdomen became firmly contracted, increasing the scaphoid appearance of this region, while the outline of the lower border of the stomach could be seen from a distance of several feet. As the thorax enlarged, cyanosis in the recumbent position disappeared.

April 15, 1921, when 4½ months old, and following a period of several days when his mother, acting on her own initiative, had left him off the board and given him a small amount of bread and milk, the baby refused the breast at the noon feeding and, shortly after, vomited several times, the vomiting being projectile in character, but without bile or fecal matter, and accompanied by cyanosis, respiratory embarrassment and collapse. A large normal stool was said to have been passed about three hours before the onset of vomiting.

Second Examination.—Examination, three hours after onset of symptoms, showed the maximum apex impulse still farther to the right than had been noted at any previous examination (outside the right nipple line). No area of tympany corresponding to the stomach could be found, nor could the outline of the greater curvature of the stomach be seen on the abdominal wall, the abdomen being scaphoid throughout. These findings, with the history, seemed to point to the entrance of at least a major part of the stomach into the left thorax.

Course.—The infant refused everything by mouth and was admitted to the hospital the following morning. Moderate cyanosis and dyspnea were present, its pulse weak and rapid, its lips dry, and there was considerable loss of turgor. Two large normal stools were passed during the day and a daily stool thereafter. Vomiting of small amounts of breast milk occurred twice during the first two days after admission—after that there was no vomiting, the infant appearing nauseated but unable to vomit. Food was taken only in small amounts, with apparent difficulty, increase of cyanosis, some dysphagia, and no appetite, signs and symptoms pointing to partial obstruction at the cardia. This was apparently confirmed by a roentgenogram made after an attempt immediately after death to introduce a barium-milk mixture into the stomach.

Death occurred during the fourth week in the hospital, after rapid loss of weight in the third, with signs of bronchopneumonia.

Permission for operation or for necropsy could not be obtained.

Comment.—What portion, if any, of the intestine was in the thorax at the time of birth cannot be known, but the acuteness of the respiratory syndrome, the displacement of the heart occurring within twenty-four hours, and the permanent alteration in contour and physical signs of the infant's abdomen, first evident coincidently with the onset of acute respiratory embarrassment, seem to indicate that the greater part of the intestine found above the diaphragm entered the thorax between the time of examination on the eighth day and the onset of severe symptoms on the ninth.

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D'ESPINE'S AND ALLIED SIGNS IN CHILDHOOD *

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About six years ago, finding that there was considerable difference of opinion as to what constituted D'Espine's sign, I looked up D'Espine's original descriptions of his "sign" and found them to be as follows:

In one article [1] he said that he had called attention briefly to this method of diagnosis in 1889,[2] and that Professor Brouardel, in a communication made for him at the session of the Academy of Nov. 8, 1904, said:

> "The first signs of bronchial adenopathy are furnished exclusively by the auscultation of the voice, and are found almost always in the immediate neighborhood of the vertebral column between the seventh cervical vertebra and the first dorsal vertebra, sometimes in the fossa 'sus-épineuse,' sometimes in the interscapular space. They consist in a quality (timbre) added to the voice, which may be called whispering (chuchotement) in the first stage and bronchophony in a more advanced stage."

He then goes on to say that:

> "It is most important to distinguish the exaggerated normal voice sound from the bronchial voice sound."

He says that:

> "The tracheal sound is heard normally through the seventh cervical spine, where it ceases abruptly. In bronchial adenopathy the bronchial sound extends downward into the space between the seventh cervical and the fourth or fifth dorsal spines. This space corresponds to the last portion of the trachea and the bifurcation of the bronchi, which is at the level of the third dorsal vertebra."

He recommends the use of "333," spoken in French, for making the test, and says:

> "If auscultation of the loud voice or cry gives no result, the child should be made to speak in a low voice."

A sound is then heard which he designates as "whispering (chuchotement)" "This sound has the same value as bronchophony."

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* Received for publication, July 31, 1922.

[1] D'Espine: The Early Diagnosis of Tuberculosis of the Bronchial Glands in Children, Bull. de l'acad. de méd. **57**:167, 1907.

[2] Manual of Picot and D'Espine, Ed. 4, 1889.

In a later communication[3] he says that:

> "The sign is most obvious when the child is made to speak or count in a low voice. The voice is then accompanied by an added whispering sound localized to one or two vertebrae, or possibly extending to the fourth or fifth. A bronchial quality to the respiration at the same place has the same diagnostic value as the whispered sound. It is necessary to be content with this, if the child is too young to speak, but the bronchial breathing is a sign of enlargement already more considerable and more extensive. It is the same with vertebral percussion."

A number of articles on D'Espine's sign have been published since that time. It is evident that their authors have not read D'Espine's original descriptions of his "sign," have not understood it, are using the term to mean something different from what he meant in his description, or that my translation of his articles is wrong. It was even suggested a year ago that D'Espine had changed his mind as to what he meant by his "sign." In order to be sure that my translation was not incorrect I sent a copy of my paper[4] to Dr. Charles Greene Cumston, an American, but also a colleague of D'Espine at the University of Geneva. He writes, "I have carefully gone over your interpretation of Professor D'Espine's sign and find it absolutely correct." I then wrote to D'Espine to find out if he had changed his mind. He answered[5] that the original description is "Aussi exacte aujourd' hui." It seems evident, therefore, that most men have not read D'Espine's original articles and are using the term "D'Espine's sign" very loosely.

The sign to which D'Espine originally called attention is, therefore, a whispering sound following the spoken voice and heard over the spinous processes. No such sound is heard normally. He believed this to be the earliest sign of enlargement of the tracheobronchial lymph nodes. He also believed that the bronchial character of the spoken voice did not normally extend below the seventh cervical spine and that extension of the bronchial sound below this point was evidence of an enlargement of the tracheobronchial lymph nodes. He considered that the extension of the bronchial voice below the seventh cervical spine was always a later sign than the addition of the whispering sound to the spoken voice and that it meant a more advanced process. He paid little attention to the character of the whispered voice (meaning by this a whisper, not the whispering sound heard after the spoken voice) and believed that extension of the bronchial respiratory sound and of dulness on percussion below the seventh cervical spine were still later manifestations and that they signified much more marked changes. Incidentally, he warns against mistaking an unusually loud or deep voice for bronchophony, and states that sometimes it is impossible to determine anything from the voice itself, because of its peculiar character or the thinness of the chest wall.

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[3] D'Espine: Brit. M. J. **2**:1136, 1910.

[4] Morse, J. L.: Am. J. Dis. Child. **11**:276 (April) 1916.

[5] Aug. 13, 1921.

In view of the great differences of opinion as to terminology, it seemed worth while to examine a series of children to determine, if possible, whether the addition of a whispering sound to the spoken voice is a normal or usual condition or not, whether this whispering sound is always added to the spoken voice before any other changes occur in the voice or respiration and where the change from the bronchial to the vesicular character of the spoken voice, whispered voice and respiration normally occurs. It also seemed worth while to try to determine whether the change from bronchial to vesicular occurred first in the spoken or the whispered voice, whether the change occurred earlier or later in the character of the respiration than in that of the voice, and the relation of dulness over the spinous processes and between the scapulae to these changes.

One hundred and eighteen patients between the ages of 2 and 14 years were studied. Seventy-five of these were between 4 and 9 years of age. Sixty-eight were boys and fifty were girls. They were consecutive cases, except that a child was occasionally missed on account of hurry or because it would not cooperate. Thirty-three of these children were brought in simply for examination and general advice and no evidences of disease were found in them. Eighteen were classified as delicate children, while thirteen had various disturbances of digestion. Six had nasopharyngitis, four had chronic disease of the tonsils and three had bronchitis. The diagnoses in the others were almost all different, not more than two or three having the same disease. The presence or absence of a whispering sound after the spoken voice was noted in each instance. In determining this point, it is necessary that the child speak sharply and that it does not make a whispering sound after speaking. "One" and "Oh" are the best words to use. The points where the spoken voice, whispered voice, and respiration changed from bronchial to vesicular were also always determined. It is evident that this is possible only when a stethoscope with a small bell is used. The point where dulness on percussion began and the presence or absence of interscapular dulness were also determined. The point of change in the character of the spoken and whispered voice and in the respiration was always definite, but there was not the same certainty about the change in the percussion note, and the findings on this point are, therefore, not quite as reliable.

In eighty-eight cases, or nearly 75 per cent., there was no whispered sound after the spoken voice; in twenty-four cases it was heard through the seventh cervical spine, and in six cases below this point as well.

It seems evident, therefore, that a whispered sound after the spoken voice is not the usual condition and is probably abnormal.

The change from bronchial to vesicular in the spoken voice took place between the seventh cervical and first dorsal spines in ninety cases and above it in nine. There was no bronchial voice anywhere in nine cases, and in four cases the character of the sound was everywhere the same and undeterminable. That is, in only six cases, or 5 per cent., did the bronchial voice extend below the seventh cervical spine.

The change from a bronchial to a vesicular whisper took place between the seventh cervical and first dorsal spines in eighty-seven instances. Three of the younger children refused to whisper. The whisper was not bronchial anywhere in five cases and the character was everywhere the same and undeterminable in one case. That is, the bronchial whisper was heard below the seventh cervical spine in twenty-two cases, or about 19 per cent.

The change from bronchial to vesicular respiration occurred between the seventh cervical and first dorsal spines in ninety-seven instances. It occurred above this point in two, in one the character of the respiration was everywhere the same and undeterminable and in three it was everywhere vesicular. In only fifteen, or less than 13 per cent., did the bronchial respiration extend below the seventh cervical spine.

The spinal dulness stopped at the seventh cervical spine in ninety-five cases and above it in one. In one other case no dulness could be made out in the neck. In twenty-one cases, or 18 per cent., therefore, there was dulness below the seventh cervical spine. Interscapular dulness was not found in any case.

In fifty-four cases there was no whispering sound after the spoken voice, the change from bronchial to vesicular in the spoken and whispered voices and in the respiration occurred at the junction of the seventh cervical and first dorsal spines, there was no dulness below the seventh cervical spine and no interscapular dulness. In eighteen others there was no whispering sound after the voice and the change from the bronchial to the vesicular sound in the spoken or whispered voice or in the dulness occurred above the seventh cervical spine. It seems fair to conclude, therefore, that when there is no whispering sound after the spoken voice, the bronchial voice, whisper and respiration and the spinal dulness do not extend below the seventh cervical spine, and there is no interscapular dulness, conditions are normal. It seems probable that they are not normal when the bronchial voice, bronchial whisper, bronchial respiration and spinal dulness extend below the seventh cervical spine. They are certainly abnormal when there is interscapular dulness.

The whispering sound after the spoken voice, which will hereafter be referred to as "D'Espine's sign," was present in sixteen instances through the seventh cervical spine and in one through the third dorsal spine, when the changes in the spoken and whispered voices, the respiration and the dulness occurred at the normal level. The diagnoses in these cases were: No disease in four cases; delicate child in five cases; asthma in two cases; cervical adenitis, indigestion, enuresis, epistaxis, hip disease and chronic disease of the tonsils, each in one case. There were twenty-nine instances in which the bronchial voice, whisper or respiration or the spinal dulness extended lower than the seventh cervical spine. In thirteen of these cases D'Espine's sign was also present, in the other sixteen cases it was not. The diagnoses in these twenty-nine cases were: No disease in five cases; delicate child in three cases; cervical adenitis, nasopharyngitis, chronic disease of the tonsils, tracheobronchial adenitis and bronchitis, each in two cases; adenoids, chronic heart disease, chronic appendicitis, congenital heart disease, tracheitis, eczema, cretinism, myocarditis, general adenitis and orthostatic albuminuria, each in one case. These abnormal signs and D'Espine's sign were at the same level in six cases, while they extended lower than D'Espine's sign in seven instances. D'Espine's sign never extended lower than the other signs, except when it was the only abnormality. The presence of D'Espine's sign in seventeen instances without any other abnormal changes would seem to corroborate D'Espine's contention that it is the earliest evidence of abnormalities in the tracheobronchial region and that abnormalities can, therefore, be discovered by it before they can by other means. If this is so, it would seem reasonable to believe that it would persist after the appearance of other signs, presumably indicative of more serious pathologic changes. It was present in thirteen instances in which there were other signs, but it was absent in sixteen cases. That is, it either does not always persist after the development of other signs or the other signs may appear without it. Either explanation is possible. It seems more reasonable to suppose, however, that the other signs may appear first, rather than that it disappears after their appearance. If so, D'Espine's contention that it is always the earliest sign of pathologic changes in the tracheobronchial region is erroneous. This detracts but little from its value, however, because in many, and, perhaps, most, instances it evidently does appear before any other signs and does furnish evidence of abnormalities which can be obtained in no other way.

The spoken and whispered voices were both bronchial below the seventh cervical spine in six instances. In these cases the change from bronchial to vesicular respiration and from dulness to a normal percussion note occurred at the same level as the change in the spoken and whispered voices. In no instance did the bronchial voice extend below the seventh cervical spine when the bronchial whisper did not extend below this level. In thirteen instances, however, the change in the whispered voice from bronchial to vesicular occurred below the seventh cervical spine when the change in the spoken voice was at the normal level. The change in the character of the respiration from bronchial to vesicular was lower than normal in six, and the dulness extended below the normal level in six of these cases. In one instance the extension of bronchial respiration through the second dorsal spine was the only abnormal sign. An extension of the bronchial sound of the whispered voice below the seventh cervical spine is more common, therefore, than that of the spoken voice. If the bronchial sound of the spoken voice is heard lower than normal so also is that of the whispered voice. It seems probable, therefore, that a change in the whispered voice takes place with slighter pathological changes in the tracheobronchial region than can be recognized by the spoken voice. The value of the change in the character of the respiration apparently lies about midway between those of the spoken and whispered voices.

Dulness on percussion over the spinous processes always extended below the seventh cervical spine when both the bronchial, spoken and whispered voices were below the normal level and in about one-half of the cases in which the bronchial whispered voice was below the normal level. It was usually at the same level as the change in the whispered voice. In two instances, however, it was lower than normal when D'Espine's sign was the only other abnormality, and in four it was the only abnormal sign. The low limit of dulness was the first dorsal in four cases, second dorsal in eleven cases, and third dorsal spine in six instances. It would seem from these figures as if the change in the percussion note is more delicate than that in the respiratory sound and that at times it may reveal pathologic changes not detectable in any other way. This may be the case, but it is somewhat doubtful, because it is more difficult to be certain of slight changes in the percussion note than in the spoken or whispered voices or in the respiration. Interscapular dulness is a relatively late sign of pathologic changes in the tracheobronchial region and, when present, signifies that such changes are considerable.

SUMMARY

The sign to which D'Espine called especial attention is a whispering sound heard after the spoken voice when the bell of the stethoscope is placed over the spinous processes. This sound is not heard under normal conditions. Normally the bronchial sound of the spoken and whispered voices and of the respiration does not extend below the seventh cervical spine. Dulness on percussion over the spinous processes stops at the same level. Extension of the bronchial sound of the spoken and whispered voices and of the respiration, as well as of dulness on percussion, below the seventh cervical spine is abnormal and has the same significance as the whispering sound after the spoken voice. The whispering sound after the spoken voice, D'Espine's sign, is often the earliest and only abnormality. It may, however, be absent when one or more of the other signs are present. The whispered voice is a somewhat more delicate test of pathological changes in the tracheobronchial region than is the spoken voice. The respiratory sound has an intermediate value. The value of percussion over the spinous processes is about the same as that of the respiratory sound. Interscapular dulness is a late sign and is found only when the pathologic changes are considerable.

A CLINICAL AND CHEMICAL STUDY OF BUTTER SOUP FEEDING IN INFANTS[*]

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Since the appearance of Czerny and Kleinschmidt's article in the *Jahrbuch für Kinderheilkunde* for 1918, describing their new butter-flour mixture for infants and their experience in its use, many contributions on the subject have appeared in the German periodicals, particularly the *Jahrbuch für Kinderheilkunde* and the *Zeitschrift für Kinderheilkunde*. The only extensive articles in English are those by Crozer Griffith[1] and by Graeme Mitchell.[2] All, with the exception of one each by Stolte[3] and Zielaskowski,[4] are mainly clinical discussions and report no metabolism observations. Most of these writers give their experience with feeding from twenty to fifty children on this food for varying lengths of time. For the type of children for whom it is indicated there is almost unanimous agreement that the use of the C-K butter-flour mixture brings about rapid and uniform weight gain, improvement in color of the skin and in turgor, deposition of subcutaneous fat, tendency to sleep well, and a generally happy disposition. The stools resemble those of breast fed infants and like them contain a large percent of fat.

Many clinicians recommend its exclusive use for very young, premature or very small infants when artificially fed. Czerny and Kleinschmidt consider that prematures under 1,700 gm. in weight should receive part breast milk. Several others think that young weakly infants should have butter-flour mixture supplemented by breast milk. One author claims to get better results with the butter-flour mixture for children over six months of age than for those under. Some report success in using it for infants who are vomiting, especially infants of the neuropathic type. There is general agreement, however, that in certain cases of eczema its use is indicated, here again with neuropathic children, while in other cases of eczema the condition is aggravated by feeding with butter-flour mixture. Several consider it adapted for long continued use, one having used it for 150 days continuously. One author reports good results with this food in intercurrent infections, another in digestive disturbances and infections when there is general weight gain. Czerny and Kleinschmidt direct its use with part breast milk in reparation from acute digestive disturbances. All seem to be agreed that it is not to be used in acute digestive disturbances with great weight loss or in decomposition or when tolerance has been lowered by infection. There is more difference of opinion regarding its use in atrophy. Several clinicians consider it not indicated, though one claims good results from its use in atrophy, parenteral infections and long continued dyspepsia. Nearly all charge the failures reported with this food to its use in too severe cases of food intolerance, and most seem to feel that it is too difficult a question for any but pediatrists to decide when its use is indicated.

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[*] From the Wards and Laboratories of the Hospital for Sick Children and the Department of Pediatrics, University of Toronto.

1. Griffith, J. P. C.: Arch. Pediat. **38**:412, 1921. Griffith, J. P. C., and Mitchell, A. G.: New York M. J. **114**:137, 1921.
2. Mitchell, A. G.: Arch. Pediat. **38**:414, 1921.
3. Stolte, K.: Jahrb. f. Kinderh. **89**:161, 1919.
4. Zielaskowski: Jahrb. f. Kinderh. **97**:330, 1922.

One author states that the butter-flour mixture gives no protection against rickets or infection; another that he has received the impression that the symptoms of rickets were worse after the use of this food, while several see no lessening in the symptoms after feeding butter-flour mixture. However, it is admitted that there is, in general, a strong tendency to rickets at present even among breast-fed infants. Stolte claims to have seen no signs of rickets, even no trace of craniotabes, after long continued use of the food.

Edema has not often been observed. When it has, it has been ascribed to an exceptionally high content of sodium chlorid in the butter used. It is also to be considered that the weak and undernourished infants among those fed on this food often show a tendency to edema on any food. The theory of a water retention as explanation of the great weight gain characteristic with this food is generally discredited. The small fluid intake in feeding butter-flour mixture and the common accompaniment of sweating are against such a theory.

One author reports success in a case of constipation when lactose was substituted for dextrose in the food. Margarine was substituted for butter by one investigator who found no ill effects whatever. A case of weight equilibrium after weeks of gaining on the food was reported when the weight curve began to rise again after addition of plasmon to increase the protein content of the food.

It is emphasized that the change to a different food must be made gradually.

The good results obtained so generally with this form of food are variously imputed to the following causes; high fat intake in a form that can be tolerated, thus covering the special need of the young infant for fat; high caloric content; low fluid content of a concentrated food; the relative proportions of fat, carbohydrate and protein resembling those of breast milk; high fat content in relation to high sodium chlorid content; the burning off of volatile fatty acids; the browning of the flour; and even the change to a gram-positive intestinal flora resembling that characteristic of breast fed infants, resulting from the use of this food.

Stolte[3] and Zielaskowski[4] give results of metabolism observations on several children fed on the C-K butter-flour mixture, to which reference will be made later. They have obtained fat and nitrogen balances and in a few cases carbohydrate and total salt balances, in one only the balances of the various salts. They found in most cases an abnormally low fat retention as per cent. of intake; normal carbohydrate retention; a positive balance of nitrogen but sometimes abnormally low retention; once a low positive salt balance and once a negative balance; and in the one case studied for retention of separate salts a negative calcium and very small phosphorus balance. They ascribe the excessive loss of calcium and phosphorus to an abnormally increased peristalsis in a neuropathic child under the restraint necessitated by the metabolism observation.

Preparation; Composition and Indication.—The original mixture calls for the following ingredients: butter (melted), 7 gm.; flour, 7 gm.; sugar, 5 gm.; water, 100 c.c. Flour and butter are always in equal amounts. The mixture is diluted with milk in the proportion of two-thirds butter-flour to one-third whole milk for children weighing less than 6½ pounds, and three-fifths butter-soup to two-fifths milk for children in a better state of nutrition. Such a food gives from seventy-five to eighty calories per pound. Even though digestion and metabolism are taxed heavily by this, contrasting as it does with the normal requirements of calories for the new-born, of sixty-five for premature babies and forty-five for older children, the food is well borne.

The foundation for recommending this feeding was the idea that the freely added fat could be tolerated better by removing the volatile fatty acids through heating; however, there is little of volatile fatty acids in good fresh butter. On the other hand, the volatile fatty acids from carbohydrate breakdown produced during digestion may disturb the process of fat digestion, more particularly when more fat is present in the food. This accounts for the fact that a digestive disturbance with the feeding runs a particularly serious course, and may easily bring about an irreparable disturbance of metabolism. Therefore, butter-flour feeding is not indicated in cases where there is a digestive or metabolic disturbance, which, however, is difficult to determine beforehand.

After considerable experimentation in the milk laboratory, the following simplified method has been adopted and used exclusively in our series of cases.[5]

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[5] We desire to thank Miss Elsie Luckam of the milk laboratory for her help in the modification of the formula.

BUTTER SOUP

Butter	7¼ level teaspoons
Granulated sugar	5¼ level teaspoons
Flour	14¾ level teaspoons
Water	17½ ounces

1. Melt the butter in a sauce pan, over the lowest possible flame, or using an asbestos mat, or until the butter stops foaming and becomes a dark color, usually taking seven minutes.

2. Add flour and sugar, blending thoroughly.

3. Add 17½ ounces of cold water and stir constantly until mixture thickens (usually taking five minutes).

4. Cook in double boiler for thirty minutes.

5. Measure and add boiled water to make 20 ounces. Normal color is light brown.

The caloric value of this butter soup (without addition of milk) is approximately 28 to the ounce. For an infant weighing seven pounds, the following feeding would thus be adopted: butter soup, 14 ounces; whole milk, 7 ounces; 7 feedings. The caloric value of this mixture is approximately 24 to the ounce.

When the stools tended to be loose, the sugar was omitted and ½ to 1 ounce of casein flour was added in order to overcome the excessive fermentation. Little difficulty has been experienced with the preparation of this food in the home.

ANALYSIS OF CASES

Private Cases.—For purposes of analysis, the series has been divided into three classes, viz., (1) new-born; (2) atrophy (marasmus), and (3) difficult feeding cases with no special symptomatology except that they would not thrive.

Series 1. New-Born.—In this series were fifteen cases with no deaths. Every infant did exceptionally well. Many of these babies were put on the diet during the first few days of life when breast milk was not available. The average age, however, at which the babies were put on the diet was approximately 6 weeks, and the average weight 7 pounds 10 ounces. The gain in weight was quite striking, the average being 2¼ pounds per month, while the best gain was 3 pounds and the lowest gain 1½ pounds per month. It will be seen from these figures that the progress was decidedly better than with the average milk and water dilutions, with which one is satisfied with a gain of one pound a month on account of the low tolerance for ordinary dilutions of cow's milk in infants at this age. The average number of calories fed to the infants in this group was 72; the highest, 84 calories per pound, only one infant receiving as low as 50 per pound. The longest period on the diet was five months.

It must be confessed that the great majority of these babies thrived as though they had been breast fed. Their tissue turgor was excellent and none of them showed any tendency to develop clinical rickets, as evidenced by the presence of craniotabes. Their stools were remarkably consistent and of a solid breast fed character. With one exception, they all tended to be constipated, thus requiring small doses of milk of magnesia. Two of these infants during the course of observation developed nasopharyngitis, which under ordinary circumstances affects the babies' progress, but in these two cases there was no appreciable clinical change in the upward progress.

Series 2. Atrophy (Marasmus).—In this group there were eighteen cases with no deaths. The average age and weight were, respectively, 3½ months and 8 pounds. The best gain was 2 pounds 11 ounces per month, while the average gain was 1½ pounds and the lowest 1 pound per month, the longest period on the diet being five and one-half months. There were four instances of craniotabes but this sign gradually disappeared under dietetic measures. No other manifestations of clinical rickets developed. There were eleven instances of nasopharyngitis, a few developing into otitis media, but as in the previous group, there was practically no change in the nutritional progress. One baby developed a severe bronchopneumonia but recovered, making a gain of 3 pounds in five months. The general progress and the number of calories fed differed very little from those in the first group.

Series 3. Infant Feeding.—In this series there were twenty cases with no fatalities. The average age was 4 months and the average weight 10½ pounds. The average gain in this series was 1¾ pounds per month, the best gain being 4 pounds and the lowest 2 pounds per month. The longest period on the diet was six months. Four cases presented definite craniotabes, in two of which it disappeared, while in the remaining two it not only persisted but definitely increased. The average caloric intake was 68 calories per pound. Seven patients in this series had infections, and in three cases there was a disposition to vomit which was not noted in the other groups. Only one patient did not do well. The general signs of improvement coincided with those of the two preceding groups.

Hospital Cases: Series 1. New-Born.—In this series there were eight cases. The average age of these infants was 7 weeks, the youngest being 2 weeks. The average weight was 4 pounds 12 ounces, the lowest being 3 pounds 1 ounce. The average caloric intake was at the rate of 82 calories a pound per day, the lowest being 60 calories and the highest 118 calories. They made an average gain of 10 ounces per month. The best gain was at the rate of 1 pound 3 ounces per month. The longest period which any of these infants were kept on this feeding was two months. Two of these eight babies lost in weight while on the feeding, and four had respiratory infections to which one succumbed. The stools were uniformly good but tended rather to be more frequent in infants of this type than in the older, heavier babies.

Series 2. Atrophy (Marasmus).—This series comprises sixteen cases, with an average age of 3 months and an average weight of 8½ pounds. The lowest weight was 5 pounds 7 ounces. They were fed on the average of 70 calories per pound of body weight, the lowest rate being 50 calories per pound and the highest 84. The most rapid gain made was 2 pounds 6 ounces a month. The average rate of gain was 1 pound 4 ounces per month and the lowest rate of gain 1 ounce per month. One case lost weight. Ten infants in this series had a respiratory infection during the period that they were on the feeding, one case had rickets when the feeding was commenced and five more cases subsequently developed craniotabes while being fed on butter soup. It was noticed especially in this type of infant that they seemed much more contented and less irritable on this feeding than babies fed on plain milk and water mixtures or even preparations of lactic acid milk and corn syrup.

Series 3. Infant Feeding.—There were twenty-seven cases in this series. The average age was 4 months; the average weight 8½ pounds, the lowest being 5 pounds 11 ounces. These babies were admitted to the hospital on account of mild respiratory infections in most instances. In fact, only six out of the twenty-seven were free of infection during the time they were on the feeding. The average gain per month was 1 pound 1 ounce. The best gain was 2 pounds 4 ounces per month, the lowest 4 ounces. Only one infant lost weight. The average caloric intake per day was at the rate of 69 calories per pound, the lowest rate being 48 and the highest 84 calories. The longest period during which a baby was kept on this feeding in the hospital was three and one-half months.

In this group, out of the twenty-seven cases, five had rickets as evidenced by the presence of craniotabes and five developed craniotabes while on the feeding. A very noticeable feature has been the steady and consistent gain in weight made during the mild and even moderately severe infections. Patients with severe bronchopneumonia were kept on the butter soup feeding throughout the illness. It would appear that this feeding was tolerated much better than simple milk and water dilutions in such cases. The stools were uniformly good throughout. No child developed diarrhea necessitating a change in the feeding.

SYNOPSIS OF CLINICAL OBSERVATIONS

In all there were 104 cases for observation (fifty-one in hospital and fifty-three in private practice). Only five babies in the entire series lost weight and did not do well. There were eight instances of mild rickets,[6] as shown by craniotabes. As is usual, those in private practice thrived better and on an average gained from ¾ to 1½ pounds more per month than the ward cases. The reasons for this are obvious.

Premature infants and those less than 3 months of age made the most substantial progress, while the reaction to parenteral infections was a most striking observation.

The caloric intake was extraordinarily high for all the series. The average was about 70 per pound, while many were given 80 and 85, and in one instance 118 calories per pound. The first sign of improvement usually noted was general comfort and reaction not unlike that of a normal breast fed baby; this was followed by improved sleep, increase in tissue turgor and color. It is worthy of note that vomiting was quite a subordinate symptom, and at no time was of a troublesome nature. In fact, it was frequently noted that infants who had previously been vomiting on simple skim milk dilutions promptly ceased on the introduction of the butter-soup feeding. The longest period for which an infant was kept on this diet was 180 days.

TABLE 1.—Retention of Fat, Nitrogen and Total Salts

	Case 1			Case 2			Case 3			Case 4		
	Fat, Gm.	Total Nitrogen, Gm.	Total Salts, Gm.	Fat, Gm.	Total Nitrogen, Gm.	Total Salts, Gm.	Fat, Gm.	Total Nitrogen, Gm.	Total Salts, Gm.	Fat, Gm.	Total Nitrogen, Gm.	Total Salts, Gm.
Intake......	29.86	2.213	2.752	27.01	2.001	2.489	27.01	2.001	2.489	21.24	1.575	1.959
Feces........	5.49	0.341	1.491	7.53	0.445	1.506	7.18	0.452	1.592	3.96	0.318	1.389
Absorbed...	24.37	1.872	1.260	19.48	1.556	0.983	19.83	1.549	0.897	17.28	1.257	0.570
Urine........	.....	1.697	0.308	.....	1.407	0.647	.....	2.296	0.942	.....	0.650	0.325
Retained....	24.37	0.175	0.952	19.48	0.149	0.336	19.83	—0.747	—0.045	17.28	0.607	0.245
Per Cent. of intake retained.....	81.6	7.9	34.6	72.1	7.5	13.5	73.4	.....	.....	81.4	38.5	12.5

With four of the children who were taking the butter-flour mixture, quantitative studies were made on the food intake and on the urine and feces. The average daily balance was obtained between intake and output of fat, nitrogen and total ash, and of some of the ash constituents. The intake, output in urine and feces and retention of fat, nitrogen and total ash are shown in Table 1. This study showed a very poor absorption of the fat of the butter-flour food, from 72.1 to 81.6 per cent. of the intake of fat, as compared with an average of about 95 per cent. for normal breast fed infants and about 90 per cent. for normal artificially fed infants. The nitrogen retention of three of the children under observation also was extremely poor, being less than 8 per cent. of the intake with two, and negative with another. The

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6. The question as to whether or not this is true rickets is discussed by Dr. Tisdall, Am. J. Dis. Child. **24**:382 (Nov.) 1922.

fourth child had an unusually large nitrogen retention, more than 38 per cent. of intake. A retention of from twenty to twenty-five per cent. of the nitrogen intake is to be expected with young normal infants doing well on breast milk or modifications of cow's milk. The retention of the total salts varied greatly in these four children. One had a large retention, two fair, while one had a negative balance of salts. These very low retention values, especially those for fat and nitrogen, appear to be inconsistent with the clinical results obtained with this food.

As previously mentioned, Stolte[3] and Zielashowski,[4] working in connection with Stolte, made some metabolism observations with butter-flour feeding. In Table 2 are found Stolte's figures which have been changed so as to represent the daily values instead of the total for the three day period as given in his table. Stolte's results are fairly comparable with those obtained in the present investigation. However, he found, on the whole, a rather higher nitrogen retention. Of his three cases, one had a small and two a large percentage retention of nitrogen. All three had a low percentage absorption of fat, two about 70 per cent. and one about 83 per cent. One had a low total salt retention and one a negative balance. The salt retention of the third was not determined. Zielaskowski found better fat absorption, only one of the four cases showing a percentage absorption abnormally low for artificially fed children. She reports only one determination of the nitrogen balance. In this case there was a high percentage retention.

TABLE 2.—Retention of Fat, Nitrogen and Total Salts (Stolte and Zielaskowski)

	Case 1 (Stolte)			Case 2 (Stolte)			Case 3 (Stolte)		Case 4 (Zielaskowski)	
	Fat, Gm.	Total Nitrogen, Gm.	Total Salts, Gm.	Fat, Gm.	Total Nitrogen, Gm.	Total Salts, Gm.	Fat, Gm.	Total Nitrogen, Gm.	Fat, Gm.	Total Nitrogen, Gm.
Intake	24.21	1.22	2.81	10.51	0.878	1.450	23.03	1.114	23.20	1.398
Feces	7.34	0.78	0.996	3.07	0.238	0.829	3.92	0.305	2.02	0.218
Urine	.....	0.30	1.707	.....	0.284	0.809	.....	0.530	.....	0.714
Retained	16.87	0.14	0.107	7.44	0.356	—0.188	19.11	0.279	21.18	0.466
Per Cent. of intake retained	69.8	11.5	3.8	70.8	40.5	.....	82.9	25.1	91.3	33.3

Since butter-flour mixture somewhat resembles breast milk in composition and produces similar clinical results the question arises why the retention values are so different with the two foods. Some points of difference in the metabolism findings may be of more or less significance. Owing to the small volume of the food given, the absolute intake of fat with butter-flour mixture is not very great, usually from 20 to 30 gm. daily. This is less than the average intake of normal breast fed infants.[7] On the other hand, the stools were much larger than those of normal breast fed babies. In the eight cases here studied the daily dried weight of the feces ranged from 8.4 to 14.2 gm., which is two or three times the average dried weight of the daily feces of normal breast fed infants. Stolte found in his three cases 13.72, 8.85 and 8.17 gm., respectively. Since the per cent. of fat in the stools of these infants averaged at least as high as that of the breast fed infants, about 48 per cent. and Stolte's 46 per cent. as compared with about 42 per cent. of the breast fed,[7] it can easily be seen how a much lower absorption of fat occurs with the butter-soup feeding.

It remains to be explained why the stools are so much larger with the butter-flour mixture. The difference in salt content, in starch content, and the difference in the nature of the fat and the protein, each or all may play a part in this connection. The nitrogen retention is less seriously affected by the large amount of the feces than the fat retention as the nitrogen excretion takes place largely through the urine. The urine, however, showed a large output of nitrogen except in the case of the youngest and smallest infant. The salt intake with butter-flour mixture is so different from that with breast milk that there is no reason to expect the same conditions as to elimination and retention of salts with the two foods.

TABLE 3.—Comparison of Butter-Flour Mixture, Breast Milk and Cow's Milk—100 C.c.

	Fat, Gm.	Protein, Gm.	Total Salts, Gm.	CaO, Gm.	MgO, Gm.	P_2O_5, Gm.	Cl, Gm.	K_2O, Gm.	Na_2O, Gm.
Butter-flour mixture ⅔ plus ⅓ milk	5.04	1.83	0.443	0.061	0.015	0.120	0.114*	0.063	0.066*
Breast milk	3.3	1.15	0.206	0.047	0.008	0.034	0.035	0.057	0.014
Cow's milk	3.5-4	3.5	0.75	0.177	0.021	0.200	0.108	0.188	0.051

* Must vary according to salt in butter used.

The differences in the amounts of the various salt constituents, between butter-flour mixture and breast milk and cow's milk, are shown in Table 3. The analyses of butter-flour mixture are those of the food as prepared at the Hospital for Sick Children. The other values are those reported by Holt.[8]

Table 4 gives the intake, output and retention of the various salts for the four children on whom the more complete studies were made. It is interesting to note the excellent calcium and magnesium retention

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[7] Holt, L. E.; Courtney, A. M., and Fales, H. L.: Am. J. Dis. Child **17**: 241 (March), 1919.

[8] Holt, L. E.; Courtney, A. M., and Fales, H. L.: Am. J. Dis. Child **10**:229 (Sept.), 1915. Steinitz, F.: Jahrb. f. Kinderh. **57**:689, 1903. Freund, W.: Jahrb. f. Kinderh. **48**:137, 1898.

TABLE 4.—RETENTION OF THE VARIOUS SALTS

	Case 1						Case 2						Case 3						Case 4			
	CaO, Gm.	MgO, Gm.	P_2O_5, Gm.	Cl, Gm.	K_2O, Gm.	Na_2O, Gm.	CaO, Gm.	MgO, Gm.	P_2O_5, Gm.	Cl. Gm.	K_2O, Gm.	Na_2O, Gm.	CaO, Gm.	MgO. Gm.	P_2O_5, Gm	Cl, Gm.	K_2O, Gm.	Na_2O, Gm.	CaO, Gm.	MgO, Gm.	P_2O_5, Gm.	Cl, Gm.
Intake..........	0.6074	0.0875	0.7972	0.6091	0.6672	0.4064	0.6307	0.0791	0.7210	0.5509	0.6034	0.3675	0.6307	0.0791	0.7210	0.5509	0.6034	0.3675	0.4965	0.0623	0.4992	0.4336
Feces...........	0.3459	0.0439	0.2776	0.0885	0.2210	0.1991	0.3706	0.0448	0.3568	0.1162	0.3849	0.2078	0.5781	0.0665	0.4300	0.0603	0.1743	0.1137	0.4030	0.0530	0.2295	0.1493
Absorbed......	0.3515	0.0436	0.5196	0.5206	0.4462	0.2073	0.2601	0.0343	0.3642	0.4347	0.2185	0.1597	0.0526	0.0126	0.2910	0.4906	0.4291	0.2538	0.0935	0.0093	0.2697	0.2843
Urine...........	0.0131	0.0114	0.2459	0.2670	0.0980	0.0233	0.0316	0.0141	0.3600	0.3240	0.2133	0.1097	0.0424	0.0164	0.4462	0.3376	0.2369	0.1770	0.0049	0.0028	......	0.2112
Retained.......	0.3384	0.0322	0.2737	0.2536	0.3482	0.1840	0.2285	0.0202	0.0042	0.1107	0.0052	0.0500	0.0102	-0.0038	-0.1552	0.1530	0.1922	0.0768	0.0886	0.0065	......	0.0731
Per Cent. of intake retained	48.5	36.8	34.3	41.6	52.2	45.3	36.2	25.5	0.6	20.1	0.9	13.6	1.6	....	....	27.8	31.9	20.9	17.8	10.4	....	16.9

TABLE 5.—COMPOSITION OF FECES

	Fat		Nitrogen		Total Ash		CaO		MgO		P_2O_5		Cl		K_2O		Na_2O	
	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight	Gm.	Per Cent. of Dried Weight
Case 1...............	5.49	45.6	0.341	2.84	1.491	12.40	0.3459	2.88	0.0439	0.36	0.2776	2.31	0.0885	0.74	0.2210	1.84	0.1991	1.66
Case 2...............	7.53	57.6	0.445	3.40	1.506	11.52	0.3706	2.84	0.0448	0.34	0.3568	2.73	0.1162	0.89	0.3849	2.95	0.2078	1.59
Case 3...............	7.18	50.7	0.452	3.19	1.592	11.23	0.5781	4.08	0.0665	0.47	0.4300	3.03	0.0608	0.43	0.1743	1.23	0.1137	0.80
Case 4...............	3.96	39.6	0.318	3.18	1.389	13.89	0.4030	4.03	0.0530	0.53	0.2295	2.30	0.1493	1.49	......	....	......	....
Case 5...............	....	57.4	.....	1.83	.....	8.87	......	2.52	......	0.32	......	2.82	......	1.53	......	....	......	....
Case 6...............	4.67	50.1	0.353	3.78	1.034	11.08	0.3424	3.67	0.0528	0.57	0.4509	4.84	0.0626	0.67	......	....	......	....
Case 7...............	5.86	55.3	0.362	3.42	1.502	13.89	0.5374	5.07	0.0665	0.63	0.2304	2.17	0.0252	0.24	0.2247	2.12	0.053	0.50
Case 8...............	3.43	40.4	0.292	3.43	1.127	13.26	0.3791	4.46	0.0487	0.57	0.1561	1.84	......	....	......	....	......	....
Case 9...............	3.73	44.6	0.245	2.93	0.900	11.84	0.3311	3.96	0.0394	0.47	0.1317	1.58	......	....	......	....	......	....

for three of the children, since there has been some question as to the adequacy of the calcium intake with butter-flour mixture. The fourth child (B) had a negligible retention of calcium, with actually a negative balance of magnesium, phosphorous, and of total salts. This was the same child which had a negative nitrogen balance. He was much older than the other children, 9½ months, though undersized. He had the largest dried weight of feces of the eight children studied. It is possible that the intake of nitrogen and of salts was not adequate in this case. A good percentage retention of sodium and chlorin was shown consistently, although the actual amount retained was not excessive in any case. In all instances, there was a large excess of inorganic acids over bases in the urine, though the total salt content of the urine varied greatly. On the other hand, the feces showed the reverse condition, the quantity of bases far exceeding that of the acids. This would seem to indicate that there must have been a relatively large amount of organic acids in the feces holding the bases in combination, thus causing a low output of bases in the urine. The ammonia content of the urine presumably was high. Unfortunately, the twenty-four hour urines were mostly amphoteric or slightly alkaline, and ammonia was not determined. The distribution of acids and bases in urine and feces with butter-flour mixture is apparently in agreement with the claim of Steinitz that with fat-rich feeding there is little alkali, much ammonia in the urine, much alkali in the feces. That the loss of bases in the stools is relatively rather than absolutely great is, however, brought out in Table 5, which gives for these nine children a more detailed study of the composition of the feces. It is here seen that with all but two of the children the mineral content of the feces both as bases and acids was fairly uniform and not actually large in amount. It is necessary to study Table 6, which gives the distribution of the fat of the feces as soap, free fatty acids, and neutral fat, in order to see how far the presence of the higher fatty acids was responsible for the excess of bases in the feces. These values were obtained by determinations made

TABLE 6.—Distribution of Fat in Feces

	Total Fat, Gm.	Fat, per Cent. of Dried Weight	Soap-Fat, per Cent. of Total Fat	Free Fatty Acids, per Cent. of Total Fat	Neutral Fat, per Cent. of Total Fat
Case 1..................	5.49	45.6	31.8	41.1	27.1
Case 2..................	7.53	57.6	44.9	33.4	21.7
Case 3..................	7.18	50.7	49.9	28.6	21.5
Case 4..................	3.95	39.6	45.1	40.4	14.5
Case 5..................	....	57.4	19.2	39.6	41.2
Case 6..................	4.67	50.1	52.6	30.0	17.4
Case 7..................	5.86	55.3	66.5	24.0	9.5
Case 8..................	3.43	40.4	54.8	30.3	14.9
Case 9..................	3.73	44.6	50.9	36.4	12.7

upon the dried feces. As the fresh stools with butter-flour feeding are distinctly acid, the soap values as obtained are necessarily higher than they would have been if determined on the fresh feces. It was observed by Holt et al.[7] that during the drying of acid feces, a portion of the fat present as free fatty acids becomes bound as soap. In the samples studied by them an average of about 10 per cent. of the total fat was found to be thus affected.

Applying this reduction to the soap values in Table 6, it is seen from the following computation that in Case 7, which had the highest percent of the total fat as soap, 66.5 per cent., only about 0.33 gm. calcium oxid could have been bound as soaps of the higher fatty acids, leaving 0.21 gm. of the calcium oxid of the feces to be otherwise held. Computation: Soap, per cent. of total fat as determined, 66.5; approximate soap, per cent. in fresh feces, 56.5; approximate amount of fat held as soap, 56.5 per cent. of 5.86 gm., or 3.3 gm.; approximate amount of calcium oxid held by 3.3 gm. stearic acid, 0.33 gm.; 0.54 gm. total amount of calcium oxid in feces, less 0.33 gm., combined with higher fatty acids, leaves 0.21 gm. calcium oxid otherwise combined. Part of this was probably excreted as phosphate, but there is then the excess of potassium still to be accounted for. Thus the acids presumably arising from carbohydrate breakdown appear to be at least equally responsible with the higher fatty acids for the calcium withdrawal in the feces. By using the same method of computation with the values for the other cases it is found that all showed a large proportion of the bases of the feces that could not be excreted as salts of the inorganic acids nor as soaps of the higher fatty acids. In only two cases, that used above as an illustration and that of the older child who had a negative nitrogen and total ash balance, was the actual loss of bases large enough to endanger the retention. In these two cases there must have been inadequate calcium addition to the body.

TABLE 7.—WATER AND CHLORIN RETENTION

	Case 1		Case 2		Case 3		Case 4	
	Water, C.c.	Cl, Gm.	Water, C.c.	Cl, Gm.	Water, C.c.	Cl, Gm.	Water, C.c.	Cl, Gm.
Intake	774	0.609	700	0.551	700	0.551	551	0.434
Feces	93	0.089	78	0.116	53	0.060	83	0.149
Urine	200	0.267	270	0.324	277	0.338	175	0.211
Retention	481	0.253	352	0.111	370	0.153	293	0.074
Per Cent. of intake retained	62.1	41.6	50.3	20.1	52.9	27.8	53.2	16.9

The possibility that the great and rapid gain in weight might be attributable to edema is no more supported by the chemical than by the clinical findings. This is shown by Table 7, giving the water balance (exclusive of losses in perspiration and respiration) and that of chlorin for the children whose total balances were obtained. Exclusive of the losses in perspiration and respiration, these four children retained from 50 to 62 per cent. of the fluid intake, or from 295 to 480 c.c. of water. Children fed on the butter-flour mixture, however, have a marked tendency to perspire freely, and these values undoubtedly must be very much reduced on that account. The chlorin retention was actually very small, though a fairly large per cent. of the intake. The chlorin content of the food, owing to the use of salted butter, is large in comparison with that of breast milk. It is not, however, much greater than that often taken in other forms of artificial feeding, in which usually a larger volume of food is taken.

Freund reports that from 0.012 to 0.159 gm. sodium chlorid, which equals from 0.007 to 0.095 gm. chlorid, are retained on breast feeding with an intake of from 0.254 to 0.329 gm. sodium chlorid, which equals from 0.152 to 0.197 gm. chlorin.

SUMMARY

1. The use of butter-flour mixture for very young and very small infants was generally attended by rapid and uniform weight gain, improvement in vigor, in tissue turgor, in disposition and in resistance to infection. Extraordinarily good results were obtained with many infants suffering from atrophy. It is not indicated, however, for children with diarrhea or other forms of severe fat or carbohydrate intolerance.

2. The caloric intake with this form of food was unusually high, averaging approximately 70 calories per pound.

3. In some cases signs of mild rickets, or a condition simulating mild rickets, were seen after continued use of butter-soup.

4. No edema was encountered.

5. If the weight became stationary after long continued use of butter-soup, the addition of protein to the food or temporary feeding with a cow's milk dilution was sufficient to bring about a continuation of the rapid weight gain.

6. The stools with this food were acid, strongly resembling those with breast milk feeding, but were much larger. Like breast milk feces they contained a high per cent. of fat.

7. There was generally a poor retention of fat and sometimes a poor retention of nitrogen and of total salts, especially by the older children.

8. There was usually a fair retention of calcium.

9. Sodium chlorid was not retained in abnormal amounts.

10. The feces contained an excess of inorganic bases over inorganic acids, and the urine showed the reverse condition. The excess of bases

in the feces was not to be accounted for by the quantity of fat excreted as soap, but apparently indicated the presence of lower acids.

11. Undoubtedly butter-flour mixture is a valuable addition to our resources in the feeding of premature, small and undernourished infants who are not suffering from any acute digestive disturbance.

The authors desire to express their gratitude to Dr. Stanley Graham, resident physician, for his analysis and synopsis of the clinical records of the hospital cases.

THE CALCIUM AND PHOSPHORUS CONCENTRATION IN THE SERUM OF INFANTS WITH MILD RICKETS OR A CONDITION SIMULATING MILD RICKETS

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Howland and Kramer[1] recently reported the results of an investigation of the calcium and inorganic phosphorus in the blood serum of infants with active rickets, and conclude that in the active stages of this disease the serum phosphorus is regularly reduced. The constant occurrence of some evidence of rickets in cases of tetany referred to by the older writers, and again recently emphasized by Brown and his co-workers[2] is now generally recognized. The calcium and phosphorus content of the serum of infants with active tetany have been determined by Kramer, Tisdall and Howland,[3] who found that the calcium was markedly reduced in all instances and in about half the cases the concentration of the inorganic phosphorus was normal or even above normal. As a result of these investigations it may be concluded that in active rickets the serum phosphorus is markedly reduced while in mild rickets associated with tetany the serum may have a normal or increased phosphate content.

Howland and Kramer[4] believe that when the product of the calcium concentration, multiplied by the phosphorus concentration expressed in mg. per 100 c.c. of serum reaches forty or more, rickets never results. When the product is less than thirty rickets always results, and when it is between thirty and forty the degree of rickets is slight or healing may occur. For instance, in an infant with active rickets in which the serum calcium is normal (10 mg. per 100 c.c.) and the phosphorus is reduced to 2.5 mg., the product equals twenty-five. Or, again, in an infant suffering from tetany with evidence of mild rickets the calcium may be reduced to about 6 mg. per 100 c.c. and the phosphorus remains normal (5.5 mg. per 100 c.c.). The product in this case is thirty-three. Another point of view is taken by Shipley, Park, McCollum and

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[*] Received for publication July 26, 1922.

[*] From the Wards and Laboratories of the Hospital for Sick Children and the Department of Pediatrics, University of Toronto.

[1] Howland, J., and Kramer, B.: Am. J. Dis. Child. **22**:105 (Aug.) 1921.

[2] Brown, A.; MacLachlan, I. F., and Simpson, R.: Am. J. Dis. Child. **19**:413 (May) 1920.

[3] Kramer, B.; Tisdall, F. F., and Howland, J.: Am. J. Dis. Child. **22**: 431 (Nov.) 1921.

[4] Howland, J., and Kramer, B.: Tr. Am. Ped. Society, 1922.

Simmonds[5] who conclude that there are two main kinds of rickets—one characterized by a normal or nearly normal blood calcium and a low phosphorus (low phosphorus rickets), and the other by a normal or nearly normal blood phosphorus but a low blood calcium (low calcium rickets). These authors base their views on the experimental production of rickets in rats.

During the past year a general investigation has been made in the wards and laboratories of this hospital on the influence on infants of "butter-flour mixture" feeding. To facilitate this study, a number of patients who were gaining rapidly on this food were kept in the hospital for a considerable time. The inorganic phosphorus in the serum of many of these patients was determined, and it was generally found to be above the average level of normal infants. In some of the patients signs of mild rickets were present (craniotabes and slight enlargement of the costochondral junctions) and in these cases the serum calcium was found to be reduced from 10 to 30 per cent. below the average level of normal infants.

The inorganic constituents of the "butter-flour mixture" feeding have been determined in connection with a metabolism study reported by Brown, Courtney and MacLachlan.[6] These investigators found that one liter of the mixture contained 0.575 gm. calcium and 0.523 gm. phosphorus. This is a much higher proportion of phosphorus to calcium than is present in either breast milk or cow's milk and it was quite suggestive that the low calcium and high phosphate in the serum was the result of the concentration of these elements in the food. It was soon found, however, that many of the infants who were kept at home, but on the same feeding (obtained from the hospital), showed no signs of rickets. This indicates that there is some other factor than the food which is responsible for the production of the signs described. It was also found that infants on other feedings who had been in the hospital for a long time had signs of mild rickets and examination of their serum showed a diminished calcium with a normal phosphate content.

In Table 1 is given the calcium and phosphate content of the serum of infants who had signs of mild rickets. Some craniotabes and slight enlargement of the costochondral junctions were present in every case. In some of the patients who were under observation for two months or more the evidences of rickets became more marked during the period of observation. The average calcium concentration was 8.8 mg. and the inorganic phosphorus content 6.1 mg. per 100 c.c. The average values found in normal infants by the methods used are 10.5 mg. calcium and 5.4 mg. phosphorus per 100 c.c. of serum.[7]

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[5] Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, N.: Am. J. Dis. Child. **23**:91 (Jan.) 1922

[6] Brown, A.; Courtney, A. M., and MacLachlan, I. F.: Am. J. Dis. Child. **24**:368 (Nov.) 1922.

The calcium and phosphate content of the serum of infants who had signs of active tetany (carpopedal spasm, laryngismus, convulsions) in addition to rickets, are given in Table 2. The diets of the infants previous to the development of the tetany are also indicated. The average calcium content found in the serum of these nine cases was 6.1 mg. calcium per 100 c.c., which compares with 5.4 mg. reported by Kramer, Tisdall and Howland [3] and 5.6 mg. by Howland and Marriott.[8] The average phosphate content found was 5.9 mg. per 100 c.c. of serum.

TABLE 1.—THE CONCENTRATION OF THE CALCIUM AND INORGANIC PHOSPHORUS IN THE SERUM OF INFANTS WITH EVIDENCES OF MILD RICKETS

Case No.	Serum No.	Age, Months	Date	Previous Diet	Length of Time on Previous Diet, Weeks	Calcium, Mg. per 100 C.c. Serum	Phosphorus, Mg. per 100 C.c. Serum
1	144	6	1/ 6/22	Butter-flour mixture	7	9.2	6.0
2	185	4	1/24/22	Butter-flour mixture	5	9.1	5.7
3	258	4	2/13/22	Butter-flour mixture	9	9.3	5.5
4	259	6	2/13/22	Butter-flour mixture	6	9.2	5.8
5	278	5	2/17/22	Butter-flour mixture	7	9.2	6.9
6	202	6	1/26/22	Butter-flour mixture	10	8.8	6.5
7	188	4	1/24/22	Butter-flour mixture	7	7.9	7.5
7	257	4¾	2/13/22	Butter-flour mixture	10	7.0	7.0
8	481	3	4/19/22	Butter flour mixture	11	8.8	6.1
9	484	..	4/21/22	Whole milk dilutions	30	9.1	4.7
10	432	18	4/ 6/22	Milk, bread, potatoes	24	9.2	6.8
11	387	4	3/23/22	Whole milk dilutions (Protein milk for 1 week)	10	9.3	5.4
Average						8.8	6.1

TABLE 2.—CONCENTRATION OF THE CALCIUM AND INORGANIC PHOSPHORUS IN THE SERUM OF RACHITIC INFANTS WITH TETANY IN ADDITION

Case No.	Serum No.	Age, Months	Date	Previous Diet	Length of Time on Previous Diet, Weeks	Calcium, Mg. per 100 C.c. Serum	Phosphorus, Mg. per 100 C.c. Serum
1	81	6	11/30/21	Eagle Brand condensed milk	21	5.4	6.7
2	186	2½	1/24/22	Breast milk and butter-flour mixture	8	7.9	6.4
3	362	5	3/10/22	(1) Whole milk dilutions followed by (2) Eagle Brand condensed milk	(1) 6 (2) 4	5.9	5.3
4	385	12	3/20/22	Breast milk...............	..	5.2	6.5
5	390	8	3/23/22	Whole milk dilutions	20	5.8	7.1
6	408	5	3/27/22	Eagle Brand condensed milk	8	7.5	5.6
7	409	9	3/27/22	Whole milk dilutions	20	5.4	5.8
8	430	11	4/ 6/22	Whole milk dilutions	40	5.0	5.8
9	431	7	4/ 6/22	Whole milk dilutions	..	6.7	3.4
Average						6.1	5.9

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[7] Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921. Tisdall, F. F.: J. Biol. Chem. **50**:329, 1922.

[8] Howland, J., and Marriott, W. McK.: Quart. J. M. **11**:289, 1918.

None of the cases reported here had what would be termed severe rickets. In some of the infants with active tetany there was a moderate enlargement of the epiphyses, while in the other cases no enlargement could be detected by clinical examination. Roentgenograms of the wrists disclosed, in the more marked cases, moderate flaring and some irregularity of the lower ends of the radius and ulna. In the other patients only the barely perceptible "fuzziness" which is generally seen in cases of tetany could be detected.

In a recent communication[9] some statements made by Hess are of considerable interest in the light of the present study. He states: "Routine blood examinations were carried out on infants who were receiving standard diets, in order to ascertain the relationship of blood phosphate to the early development of rickets . . . in general it was found that clinical rickets may precede a decrease in the inorganic phosphate of the blood but that the later roentgen-ray signs were accompanied usually by a low blood phosphate." However, no calcium determinations were reported. It is quite possible that the mild cases that Hess observed were cases of rickets of the type associated with a normal phosphate concentration in the blood serum and a diminished calcium concentration.

In the same communication Hess states that the blood of infants apparently free from rickets, according to all recognized signs and symptoms, may be low in inorganic phosphate. After making several hundred determinations of the inorganic phosphate content of serum of normal infants, and others suffering from various pathologic conditions, I am convinced that a diminished inorganic phosphate content of the serum does not occur in normal infants or at least is extremely rare. It is possible that the difference between the results recorded by Hess and the above results is due to the different methods used, or to the fact that his determinations were made on whole blood, while the present ones were made on blood serum. As the inorganic phosphate content of corpuscles and serum are not identical, and as it is the serum and not the corpuscles which tends to be in equilibrium with the tissue fluids, it is probable that the phosphate content of the serum is of more value than that of whole blood.

The question may be raised whether the patients without tetany were really suffering from rickets in the true sense of the word. The product of the average calcium and phosphorus concentration in the serum of these infants is fifty-three. According to Howland and Kramer's view, there should have been no evidence of rickets, as the product of the concentration of the calcium and the phosphorus is well above forty. In these infants the clinical evidence of rickets consisted only of craniotabes and slight enlargement of the costochondral junctions. Schwarz,[10] Unruh,[11] Feer[12] and others considered these signs diagnostic of rickets and concluded that this disease occurred in from 50 to 80 per cent. of newly born infants. Schmorl,[13] who is probably one of the greatest authorities on rickets, conducted an extensive investigation of the disease and found no microscopic evidence of rickets in the bones until the second month of life. Thus it is clear that these signs alone cannot be taken as evidences of true rickets. Park, Shipley, McCollum and Simmonds[14] have found that diets very high in phosphorus and very low in calcium produce changes in the bones of rats which differ from rickets. "The bones were thin. The enlargement of the costochondral junctions and ends of the long bones were slight or lacking. Fractures were not found." In view of these facts, the possibility must be considered that the bone change which accounted for the craniotabes in our patients, without definite involvement of the long bones, might be more of an osteoporotic nature than true rickets.

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[9] Hess, A. F.: J. A. M. A. **78**:1177 (April 22) 1922.

CONCLUSIONS

1. The calcium and inorganic phosphorus concentration in the serum of a number of infants with craniotabes and slight enlargement of the costochondral junctions averaged 8.8 mg. calcium and 6.1 mg. phosphorus per 100 c.c. of serum. The average values found in normal infants by the methods used are 10.5 mg. calcium and 5.4 mg. phosphorus per 100 c.c. of serum.

2. The average concentration of the calcium and inorganic phosphorus in the serum of a number of infants with signs of active tetany in addition was 6.1 mg. calcium and 5.9 mg. phosphorus per 100 c.c. of serum.

3. The question is raised whether the bone changes observed (craniotabes and enlargement of the costochondral junctions) were not more of an osteoporotic nature than true rickets.

I wish to acknowledge thanks to Dr. Alan Brown, physician-in-chief, for permission to report these cases.

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[10] Schwarz, F.: Med. Jahrb. **2**:495, 1887.

[11] Unruh: Jahresb. d. Gesellsch. f. Nat. u. Heilk. in Dresd. **53**:1886.

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[13] Schmorl, G.: Ergebn. d. inn. Med. u. Kinderh. **4**:403, 1909.

[14] Park, E. A.; Shipley, P. G.; McCollum, E. V., and Simmonds, N.: J. Biol. Chem. **50**: VII, 1922.

THE INCIDENCE OF MENINGITIS IN EARLY INFANCY, WITH A DESCRIPTION OF TWO CASES DUE TO UNUSUAL ORGANISMS *

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Although meningitis is common in childhood, it is rather infrequent in early infancy and relatively few instances have been described in infants under 3 months of age. This may be due, in part, to the relative isolation of young infants and the consequent lack of opportunity for infection. A variety of micro-organisms has been associated with meningeal infections, and it is of interest that certain of them have been particularly associated with meningitis in early infancy while infection with other types of organisms has been relatively rare. It is also noteworthy that certain types of bacteria which not infrequently cause meningitis in early infancy are rarely associated with such infections later in life. In this paper are reported two instances of meningitis in young infants caused by organisms of this latter type. In addition we have observed four cases of meningococcus meningitis (cerebrospinal fever), two others due to the streptococcus and two to the pneumococcus. All were in children under 3 months of age. Before describing the cases we have observed, we will review briefly the incidence of meningitis in infants under 3 months of age.

Meningococcus.—While it seems likely that all instances of meningococcus meningitis in early infancy have not been reported, we have been able to find only twelve cases[1] in the literature of the past five years. Even assuming the existence of an equal number of similar unreported cases, the rarity of infection in early life as compared with the incidence later is apparent. In thirty-five consecutive cases of meningococcus meningitis admitted to the St. Louis Children's Hospital in children under 2 years, four were under 3 months of age. This is a relatively high proportion and, we believe, the occurrence of the infection in early infancy is, in general, much more infrequent than

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[1] Koplik, H.: (4 cases), Arch. Pediat. **33**:481 (July) 1916; White, T. W.: (1 case), Arch. Pediat. **34**:372 (May) 1917; Acuña, M., and Casaubon, A.: (3 cases), Arch. de méd. d. enf. **21**:169 (April) 1918; Ugon, A.: (1 case), Arch. Lat. Am. de Pediat. (Nov. and Dec.) 1918; abstr. in Arch. de méd. d. enf. **22**:557 (Oct.) 1919; Castro, R.: (1 case), Arch. Lat. Am. de Pediat. (March and April) 1920; abstr. in Arch. de méd. d. enf. **23**:555 (Sept.) 1920; Gutierrez, A. C.: (1 case), Arch. Españoles de Pediat. **4**:385 (July) 1920; Rémy, A., and Caussade, L.: (1 case), Paris méd. **11**:129 (Feb. 12) 1921.

indicated by these figures. It seems more reasonable to attribute the low incidence in very young infants to their isolation rather than any immunity to this infection.

The first case, the youngest observed, was a fulminating infection in an infant, 17 days old, accompanied by an extensive petechial rash. The organism isolated was identified as a parameningococcus by agglutination tests. This variety of the meningococcus appears to be the more common one in St. Louis since of seven strains isolated and identified from this and other cases of cerebrospinal fever, only one was the regular or normal meningococcus, the rest being parameningococcus. The second case was in an infant, 10 weeks of age, seen rather late in the disease which was uninfluenced by serum treatment. The other two cases were in infants, 2 months old, who recovered, although one developed a hydrocephalus. It is of interest that these four cases furnish examples of all the usual clinical forms of cerebrospinal fever in infancy: (1) the fulminant, rapidly fatal type, with extensive petechial rash; (2) the rather severe form which is not treated until the second week and which is little affected by specific therapy; (3) the infant also treated somewhat late who recovers with a chronic basilar meningitis and hydrocephalus, and (4) apparently complete recovery under serum treatment with no hydrocephalus or other apparent residue of the infection.

Bacillus tuberculosis.—Tuberculous meningitis, frequently an incident in a general miliary tuberculosis, is also relatively rare in early infancy. Holt,[2] in a series of 218 cases of tuberculous meningitis in children under 3 years of age, found only three cases in infants less than 3 months old. The low incidence in early infancy is due, in part, to the lessened opportunity for infection that the relative isolation of this age gives. There is probably another factor which contributes to the small number of cases observed. Tuberculous meningitis is always secondary to some focus of tuberculosis elsewhere in the body. Although the marked susceptibility of infants to tuberculosis and the relative rapidity with which the infection may spread are recognized, nevertheless, a certain period of time is required after infection for the development of the initial lesion, and for the metastasis to the meninges to occur. It is not surprising that in only occasional instances the development of the infection is sufficiently rapid for meningitis to result in early infancy. We have seen no case under 3 months of age.

Bacillus influenzae.—In a series of forty-nine cases of meningitis caused by the Pfeiffer bacillus collected by Wollstein,[3] three of the patients were noted as being under 3 months of age, although four infants whose age was not given were designated "nurslings," and may have been very young infants.

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[2] Holt, L. E.: Observations on Three Hundred Cases of Acute Meningitis in Infants and Young Children, Am. J. Dis. Child. **1**:26 (Jan.) 1911.

[3] Wollstein, M.: Influenzal Meningitis and Its Experimental Production, Am. J. Dis. Child. **1**:42 (Jan.) 1911.

Recently Neal[4] reported thirty-two cases of which two were in infants under 3 months old, and of twenty-three cases reported by Rivers,[5] one child was under 3 months. About half of all reported cases occurred during the first year of life. The only case we have observed was in a 5 months old infant in which the meningeal infection was apparently primary. The organism isolated was typical.

Streptococcus, Staphylococcus, and Pneumococcus.—Purulent meningitis from these common pyogenic cocci is apparently somewhat more frequently observed in early infancy than the form due to the other organisms mentioned. Barron[6] has collected from the literature fourteen cases, six due to the streptococcus and staphylococcus, four to the streptococcus alone and four to the pneumococcus. Four of these infants had spina bifida. It is likely that a considerable percentage of the others may have been associated with the extension of an infection from the middle ear and mastoid, or with pneumonia since this is true in older infants.

Of thirty cases of purulent meningitis from pyogenic cocci observed in the St. Louis Children's Hospital, half the patients were under 2 years of age and four were under 3 months old. In two of these young infants the meningitis was caused by a streptococcus and in two by a pneumococcus. The streptococcus infection in one infant (22 days old) was associated with a spina bifida and in the other (2 months old) with a brain abscess. One of the cases of pneumococcus meningitis was of the group usually called "primary" and was immediately preceded by an acute follicular tonsillitis and rhinopharyngitis, while the other accompanied an empyema. Both infants were 2 months of age. The association of purulent meningitis with middle ear and mastoid infection, due to these pyogenic cocci, is not uncommonly noted in childhood but we have not observed a case of this type in early infancy.

Colon Bacilli and Allied Intestinal Bacteria.—It is this group of organisms that is of particular interest with relation to meningitis since such infection is apparently peculiar to very young infants. Eighteen cases were collected by Barron[6] of which fifteen were in infants under 3 months of age and of the other three one child was 4 months old and two were 5 months old. The organisms isolated were *B. coli* in fourteen cases; *B. lactis aerogenes, B. mucosus capsulatus, B. pyocyaneus* and

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[4] Neal, J. B.: Influenzal Meningitis, Arch. Pediat. **38**:1 (Jan.) 1921.

[5] Rivers, T. M.: Influenzal Meningitis, Am. J. Dis. Child. **24**:102 (Aug.) 1922.

[6] Barron, M.: Meningitis in the Newborn and in Early Infancy, Am. J. M. Sc. **156**:358 (Sept.) 1918.

B. typhosus, each in one instance. Since this report Greenthal[7] has observed a case of meningitis in an infant one month old which was due to *B. acidi lactici.* Smith and Aberd[8] have isolated *B. enteritidis* (Gaertner) from the meningeal exudate of a 5 weeks old infant, and Sherman[9] has reported a newly-born infant with *B. acidi lactici* meningitis. It is rather striking that meningeal infection by organisms of this group is so sharply limited to early infancy since apparently similar cases are seen rarely, if at all, in late infancy and childhood.

We have observed two instances of infection in young infants with organisms of this type. The first case was in an infant 10 weeks old with meningitis due to a colon-like bacillus which was agglutinated by the patient's serum. Intraventricular injections of the patient's serum were without apparent influence on the course of the infection. The second case was in an infant 4 weeks old with hereditary syphilis who developed a purulent meningitis caused by an encapsulated bacillus not corresponding to any previously described micro-organism.

REPORT OF CASES

Case 1.—*History.*—N. W., a white male infant, 10 weeks of age, was admitted to the St. Louis Children's Hospital, June 16, 1921, with the complaints of malnutrition, irritability and constipation. The parents were in good health and had no other children. The baby had been delivered by a midwife and was said to have weighed 9 pounds at birth which was spontaneous and at term. It had never been nursed but had been fed at two hour intervals on a dried milk preparation. Frequent enemas had been given on account of a persistent constipation. Vomiting had followed many of the feedings and had been present since birth.

Examination.—On admission, the examination showed a moderately atrophic infant weighing 3,200 gm. with a temperature of 37 C., not acutely ill. The head appeared to be somewhat large; there was some fulness of the anterior fontanel, and the sutures were slightly separated. In addition, the neck was moderately retracted and stiff. On bending the neck forward there was a slight flexion of the thighs, but Kernig's sign was absent. Aside from some increased irritability on being handled, the physical examination was otherwise negative. The leukocytes numbered 28,800. On lumbar puncture 15 c.c. of a greenish yellow turbid fluid was removed which showed 15,000 cells per c.c. with 87 per cent. polymorphonuclears. Gram-negative rods in fair numbers were present in smears and grew in pure culture from this as well as all successive puncture fluids. Their cultural characteristics will be discussed later.

Course.—During the following six days, the patient's condition remained practically unchanged, although frequently there was moderate vomiting after feeding, and gradual loss of weight. The fontanel became more tense but from a second lumbar puncture no fluid was obtained. Since it had been found that the organism isolated from the first puncture fluid was agglutinated by the patient's serum in dilutions of 1:80, 10 c.c. of the patient's serum was injected into the ventricle. No effect from this injection was observed. Two days later the infant had a convulsion which lasted less than a minute, and another ventricular puncture was done with the introduction of 10 c.c. more of the patient's own serum. This was followed by slight improvement, but the child had several more convulsions and died the next day—nine days after admission. During observation in the hospital the temperature varied between 36 and 38 C. The urine was negative. The Pirquet and the Wassermann reactions were negative.

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[7] Greenthal, R. M.: Case of Meningitis Due to the Bacillus Acidi Lactici, Am. J. Dis. Child. **21**:203 (Feb.) 1921.

[8] Smith, J., and Aberd, M. D.: Gaertner Meningitis Complicating Gaertner Enteritis, Lancet **2**:705 (Oct. 1) 1921.

[9] Sherman, De W. H.: A Peculiar Case of Purulent Meningitis in the Newborn, Tr. Am. Pediat. Soc. **34**:192, 1922.

Diagnosis.—Purulent meningitis due to a paracolon bacillus; internal hydrocephalus (secondary) and athrepsia.

Necropsy Report.—A complete necropsy was performed which confirmed the foregoing diagnoses. The body was much emaciated and weighed 2,800 gm. A rather thick fibrinopurulent exudate covered the brain. The ventricles were moderately dilated and contained pus. Sections showed the exudate to be composed of much fibrin, many polymorphonuclear and both large and small mononuclear leukocytes. There was a well marked perivascular infiltration also. Through the lungs were scattered small areas of a dark red color which, on microscopic examination proved to be patches of atelectasis and early pneumonia. The intestines were free from anatomical abnormalities. Other details of the necropsy protocol will be omitted since nothing of special interest was revealed.

Anatomic Diagnosis: fibrinopurulent meningitis and ependymitis; internal hydrocephalus; lobular atelectasis; commencing bronchopneumonia; emaciation.

BACTERIOLOGY.—The cerebrospinal fluid removed from the spinal puncture and from the two ventricular punctures during life and that found in the ventricles at necropsy was purulent, of a greenish yellow color and had a faint odor of putrefaction. Microscopic examination showed many pus cells and gram-negative rods resembling colon bacilli. They were extracellular. Cultures from the puncture fluids and those made postmortem showed an abundant pure growth of the same organism.

Serum from the patient taken five days before death gave complete agglutination of the organism in dilutions of 1:20, 1:40 and 1:80, but did not agglutinate *B. typhosus, B. paratyphosus A, B. coli-communior* in dilutions of 1:20. The organism isolated from the patient was not agglutinated by pooled normal human serum.

The organism was motile, methyl red test positive, and Voges-Proskauer test negative. Indol was produced. Gelatin was not liquefied. Milk became slightly acid and was coagulated on the second or third day. Acid and gas were formed from dextrose, saccharose, mannite, xylose, maltose, arabinose, glycerol, galactose, adonite, levulose and sorbitol. Acid and gas production from salicin and rhamnose was delayed. Acid production from lactose was delayed and no gas was produced. Raffinose, dextrin, inulin, starch, dulcitol, amygdalin, inositol, and erythritol were unaffected.

The medium used was 1 per cent. peptone, 0.4 per cent. dibasic sodium phosphate, and Bronfenbrenner's indicator, with Durham fermentation tubes. Hiss' serum water was also used. Sugars were used in 1 per cent. strength. The media with most sugars was filtered through a diatomaceous filter and was not heated. Cultures were incubated ten days.

Cultures from the heart's blood were sterile.

CASE 2.—*History.*—Baby A., colored, female, was first seen Sept. 26, 1921, at the age of 10 days when brought to the Washington University Dispensary with the complaint of a rash on the hands and feet which had appeared four days previously. The mother had had two miscarriages and her blood, taken two weeks before the birth of the patient, showed a strongly positive Wassermann reaction. It was stated that the birth-weight was 5 pounds and that the infant had been fed at the breast every two hours and appeared to be well with the exception of the skin trouble.

Examination.—On examination, the patient was a poorly nourished infant with enlarged epitrochlears and a large liver and spleen. Both feet and both hands were covered by large bullous lesions.

Course.—Daily inunctions of mercury were prescribed and breast feedings at three hour intervals. During the following two weeks the baby was seen several times and the skin lesions were regressing, although the nutrition remained unsatisfactory. Oct. 13, 1921, when 4 weeks old, the infant was brought to the clinic with the history that convulsions had begun the previous day and recurred at intervals since. The temperature was 35.8 C., and the baby was having rather frequent general convulsions. The sclerae were considerably jaundiced, a symptom which had not been noted previously. Lumbar puncture showed a yellow turbid fluid under increased pressure containing 1,500 cells, most of which were polymorphonuclears. The supernatant fluid after centrifugation was golden yellow and gave a strong test for bile. The Wassermann reaction was strongly positive on 0.4 c.c. In stained smears from the sediment rather numerous gram-negative rods were seen within the cells. The convulsions continued and the baby died several hours later. No necropsy was obtained.

Diagnosis.—Hereditary syphilis; acute purulent meningitis; jaundice.

BACTERIOLOGY.—A gram-negative bacillus with morphology similar to *B. coli* was present in stained films from the purulent cerebrospinal fluid and was recovered in pure culture. Many of the bacilli were intracellular.

The organism has been studied thoroughly by one of us (H. H. B.), but only a summary of the more important characteristics will be given. In morphology it closely resembles *B. coli* and shows similar variations in size, although most of the individuals are fairly uniform. It is readily stained by all the usual dyes, and is decolorized by Gram's method. Spores are not produced. The growth is aerobic and facultative anaerobic, and abundant on all media. Gelatin and Loeffler's blood serum are rapidly liquefied, and litmus milk is quickly peptonized with little change in reaction. Growth occurs at room temperature almost as well as at 37 C. The organism is nonmotile.

On all solid mediums the growth is very tenacious and elastic. It is drawn out by the needle and when broken snaps back like an elastic band. In broth, a mucoid, flocculent sediment forms with diffuse clouding of the medium. This stringy substance is precipitated by dilute acid and is probably mucin, although its further identification was not attempted.

Indol is produced in very small amount as shown by the vanillin test, but the cholera red and paradimethylamidobenzol tests are negative.

No fermentation with gas production occurs in any of the sugars mentioned in the description of the organism from Case 1. With some of these sugars small amounts of acid were produced which changed the p_H from 7.5 to from 7.0 to 6.6, but the acidity never went below this latter point. Quantitative tests showed a disappearance of a very small amount of the sugar after ten days' incubation. Such reactions, however, are not at all comparable to the usual carbohydrate fermentation by members of the colon group.

Rabbit and guinea-pig inoculations were without effect, but intraperitoneal inoculation with a mouse caused death in twelve hours. The peritoneal exudate was mucoid with numerous organisms which showed a small capsule by Hiss' method.

The organism described is distinguished from the encapsulated colon-aerogenes group, mucosus capsulatus and hemorrhagic septicemia group by being very proteolytic and by other characteristics. The most conspicuous peculiarities, in addition to its great proteolytic action, are its inability to attack sugars energetically with marked acid production and the elastic character of its growth. In view of the latter peculiarity we propose the name *Bacterium elasticum* to distinguish it from the other species of encapsulated organisms already described.

DISCUSSION

The occurrence of meningitis in early infancy apparently depends on several factors. The four cases of meningitis due to the meningococcus present no essential differences from instances observed later in childhood and it seems likely that the low incidence in the early months of life is due almost entirely to the relative isolation of the very young. Purulent meningitis caused by such pyogenic organisms as streptococci and pneumococci, as illustrated by the instances we have observed and others in the literature, also differs little in its pathogenesis, whether occurring in early infancy or later with one exception. Infants with spina bifida in which the covering of the sac is thin, may be infected as a result of trauma to the tumor and the direct extension of an infection of the skin. In this condition the dura is cleft, as well as the vertebral laminae, and does not cover the sac, the arachnoid being immediately beneath the skin. Otherwise, such purulent meningitis both in early infancy and later is secondary to other pyogenic inflammations either by direct extension, or from otitis media, or brain abscess, or transmission by the blood from a pneumonia or other more or less distant suppuration. Any decrease in the incidence of such purulent meningitis in early infancy may be attributed merely to the fact that severe suppurative and inflammatory lesions are more common later than in the earliest months of life. In contrast to the types of organisms already mentioned, however, are those cases of meningitis in young infants caused by the group of colon bacilli and other gram-negative bacilli of the intestinal tract. These infections form a distinct group peculiar to the newly-born and infants in the early months of life and do not occur in older children. We have observed two cases of this variety. The clinical symptoms of the different varieties of meningitis seen in early infancy have shown nothing especially characteristic or strikingly different from similar infections in later infancy and childhood.

The cases of meningitis due to intestinal bacteria have especially interested us from the standpoint of the organisms involved and the origin of the infection. Most of the organisms mentioned in connection with these cases and designated *B. coli* have not been described in sufficient detail to determine definitely their identity. It may be possible that certain members of the colon group are particularly associated with meningitis in infancy but this can only be determined by a comparison of detailed descriptions of the cultures isolated. Because of the multiplicity of types and the differences in classification of this group, considerable detail in description of strains isolated from such cases would be of value. On the other hand, it is evident, even from the relatively meager reports, that the meningeal infection may be caused by any one of several more or less distinct varieties of bacteria found commonly in the intestinal tract and not ordinarily considered capable of a virulent invasion of the body. In the instances we have observed, the organism isolated from the first case obviously belongs to the large number of bacteria intermediate between the typhoid and colon groups, but differs in minor details from other species previously described. The organism in the second case is strikingly peculiar and belongs to a capsulated group of bacteria. It differs, however, from the mucosus capsulatus group and from the hemorrhagic septicemia group by being very proteolytic and in other respects. It is apparently a distinctly new type of organism and we propose to designate it *Bacterium elasticum* from the elastic character of the growth in culture.

The origin of the meningeal infection in these cases is somewhat obscure since, in practically all the instances observed, no other focus of infection has been present. These cases are termed, therefore, "primary" meningitis. On account of the type of bacteria involved it is, perhaps, a natural assumption that the organisms were derived from the intestinal tract and reached the meninges through the blood. Direct evidence in proof of such an explanation is difficult to obtain, but it is of interest to see how certain known phenomena give indirect evidence to support this hypothesis. Three factors are apparently involved in the production of purulent meningitis by intestinal bacteria. These are: (1) the greater permeability of the intestinal mucosa in early infancy; (2) the decreased resistance of young infants to bacterial infection associated with defective antibody formation, and (3) the influence of digestive disturbances and malnutrition on the above mentioned factors.

The permeability of the adult intestinal mucosa for bacteria of the colon group is well known from the ease with which they may be demonstrated in the mesenteric lymph nodes and even in the liver. These organisms, however, appear to be destroyed by the body without the production of any evidence of infection. The fact that the serum of most persons contains agglutinins for colon bacilli—the so-called "normal" agglutinins—is usually attributed to this more or less constant passage of these bacteria into the body, while the infrequency of infections is ascribed to the presence of acquired immune substances of which the "normal" agglutinin is an example. It has been shown by von Behring[10] that the intestinal mucosa of young animals is more permeable to bacteria and to foreign proteins than that of older animals.

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[10] Von Behring, E.: Einführung in die Lehre von der Bekämpfung der Infektionskrankheiten, Berlin, Hirschwald, 1912, p. 371.

Similarly, Lawatschek[11] has demonstrated that in young infants foreign protein may pass through the mucosa of the intestine unchanged and may be recognized in the urine by the precipitin test. It seems, therefore, a justifiable assumption that in early infancy the permeability of the intestinal mucosa for colon bacilli and allied organisms is increased.

There are a number of observations regarding the lack of production of antibodies by young animals and by infants. One instance is the absence of complement-fixing substances in tuberculosis of infants in the first year of life[12] although such substances appear in a considerable proportion of older children with the infection. Isohemagglutinins, also, are usually absent in the serum of the newly-born infant. Although it has been shown experimentally that newly-born animals may inherit recognizable amounts of certain immune substances, such as hemolysins and agglutinins by their transmission through the placenta, this occurs only when the mother's serum contains a fairly high concentration of these antibodies. The concentration of normal agglutinins for the colon group, however, is relatively low, and the serum of new-born animals contains none of these normal agglutinins. Since these substances can readily be demonstrated later in life, they are assumed to be an evidence of an immunity acquired by the absorption of bacteria from the intestinal tract. Their absence in the early months of life, therefore, may be associated with a lowered power of resistance to infection by members of this group.

The relation of malnutrition and digestive disturbances in infants to infection is little understood but it is generally recognized that infants who are poorly nourished are definitely more susceptible to infections. The greater the degree of athrepsia, the lower the resistance appears to be. In both cases observed by us the nutrition was poor, one infant being moderately athreptic, from improper feeding, and the other suffering from hereditary syphilis, a disease which is not infrequently associated with malnutrition and greater susceptibility to other acute infections. It seems likely that the poor nutrition in these cases may have been one of the factors that was concerned in the production of these meningeal infections.

SUMMARY

The incidence of acute meningitis in infants under 3 months of age is briefly reviewed with mention of four cases due to meningococcus, two to streptococcus and two caused by pneumococcus observed in early infancy. Two cases are described in which the organisms involved were gram-negative bacilli of the type commonly found in the intestinal tract. One of these belonged to the group of paracolon bacilli, but did not correspond exactly in fermentation reaction to other described strains, while in the second case the organism isolated was an encapsulated proteolytic nonfermenting bacillus apparently not hitherto observed. On account of the tough elastic growth on culture mediums, we have suggested the name *Bacterium elasticum* for this organism.

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[11] Lawatschek, R.: Die enterale Resorption von genuinem Eiweiss bei Neugebornenen und darmkranken Säuglingen und ihre Ververtbarkeit als Funktionsprüfungsmethode, Prag. med. Wchnschr. **39**:185 (April 16) 1914.

[12] Cooke, J. V.: Complement Fixation for Tuberculosis in Children, Am. J. Dis. Child. **21**:78 (Jan.) 1921.

The fact that meningeal infection with colon bacilli and allied organisms is usually unaccompanied by recognizable infection elsewhere in the body suggests that these bacteria gain entrance through the intestine. The possible relation of various factors in explaining why such infections are confined to early infancy is discussed, and reasons given for the belief that the increased permeability of the intestinal mucosa to bacteria, the absence of inherited immunity to the colon group, the imperfect power of antibody formation in young infants, and the general lowered resistance accompanying malnutrition predispose to infection by organisms of this type.

A STUDY OF THE SHADOWS IN THE THORAX OF THE NEWLY-BORN *

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This study was undertaken with the hope of devising some method by which the abnormal shadows in the thorax of the newly-born could be differentiated from the normal ones. At the onset we appreciated that we had undertaken a problem of greater magnitude than we had expected. The deeper we went into the subject the greater was the variance in the shadows that we found could exist without causing any clinical symptoms. It was soon fully appreciated by us that it would require the study of a large series of cases before any attempt could be made to declare the normal to be such, and further we became more forcibly convinced that the normal shadows would first have to be determined before the abnormal could be recognized.

In presenting the observations of the study we do so in the form of a preliminary report.

Our study is based on observations made in a series of fifty-two newly borns. It included careful physical examinations and accurate measurements of all the cases examined, which cases were consecutive in the Newly-Born Service at the Touro Infirmary, and were not selected. Every baby was roentgenographed within the first forty-eight hours after birth with one exception, a premature, whose observations were made when he had reached 3 pounds, 14½ ounces. In none of the cases in this series was there a heart murmur, and in none was there any clinical evidence of an enlarged thymus. In no instance was there the slightest indication of inconvenience to the patient nor of interference in his normal progress following the making of the roentgenogram. We have not been able to find in the literature any studies made on the small child such as we were to make, and hence had nothing to start from. The methods devised by the workers in the adult investigations of the heart we found could not be employed in our study. In the adult the heart shadow is fixed and the normal may readily be recognized and any deviation therefrom determined. In the infant, and especially in the newly-born, the influence of development and growth, the transition from intra-uterine to extra-uterine life, and the rotation and change of position of the heart in the thorax with the intimate relation of the thymus make the problem a more difficult one.

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* Received for publication May 25, 1922.

The plan of measuring the size of the heart, as shown in roentgenographic studies in the adult, are not of much value in the infant. Because of the changes which occur in the thorax at this time of life, it seemed to us that by studying the size of the heart shadow in its relation to the size of the thorax we could make some headway. It was soon shown, however, that the heart shadows varied so that this method would not suffice. We found that there were several distinct types of heart shadows. It may be possible to consider each type of heart shadow separately in a sufficiently large number of cases and secure some definite information, as well as it would be of interest to attempt to ascertain the explanation for these different types.

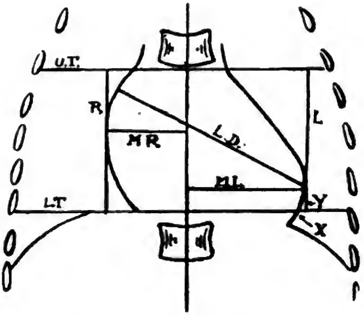

Fig. 1.—Scheme of Measurement.

In this study we employed a method of measurement in which the size of the shadow of the heart was determined by a square within which its shadow could be included. A line, L. T. = lower transverse, is drawn horizontally across the thorax at the level of the upper margin of the diaphragm. A line, U. T. = upper transverse, is drawn in like manner horizontally across the thorax at the level of the upper border of the heart. Two lines, R. and L. R. = right vertical, extending vertically and at right angles from L. T. to U. T. at the right margin of the heart; and L., a similar line at the left margin of the heart; M. = median line drawn to correspond to the center of the vertebral column; M. R. = line from the median line M. to the right margin of the shadow of the heart; M. L. = line from the median line to the left margin of the shadow of the heart; L. D. = largest dimension of the heart, a line drawn from its apex to its base; X = distance from the left border of the heart shadow to the point of mergence of the heart shadow and the diaphragm; Y = distance on L. from L. T. to left border of shadow of the heart.

Owing to our inability to make exposures at the normal working distance of 2 meters, which distance is used in the adult, we do not attempt to offer the exact measurements of the heart but only the relative size of the heart shadow in its relation to the size of the thorax. The advantage of the 2 meter working distance is that it eliminates the magnification of the shadow and only the normal roentgen ray is employed.

In our observations the technic of making the roentgenograms was as follows: The baby was placed in the recumbent position; a double intensifying screen carrying a duplitized film was used; the opening in the diaphragm (12 cm.) of the tube carriage was centered over the cardiac area at a working distance of 26 inches, and 110 milliamperes of current with a backup of 3½ inches was used and an exposure of one-tenth second made. This time factor was regulated by an automatic timer.

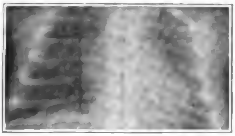

Figure 2

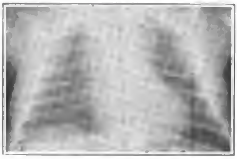

Figure 3

Fig. 2.—Serial No. 1. Radiograph No. 31089. Baby's weight, 8 pounds 12½ ounces. Globular heart, typical. Heart position negative. Thymus to left.

Fig. 3.—Serial No. 7. Radiograph No. 31842. Baby's weight, 7 pounds 10 ounces. Adult heart, typical. Heart to left. Thymus to right and left.

The types of heart and the incidence of each type, as determined by the shadows, were as follows: Globular in twenty-one instances; adult in seven instances; drop in five instances; nutmeg in three instances; square in two instances; round in one instance; unusual in one instance; unclassified in ten instances.

The unclassified heart shadows are so grouped because insufficient clearness of outline would not permit of our conscientiously placing them in any of the groups mentioned.

The globular type showed variations both as to size and position. The smallest was in the smallest infant weighing 3 pounds, 4 ounces, and interesting to relate the position of the heart was exactly centrally located, the M. L. and M. R. measurements being the same. The largest heart shadow of this type, however, was not found in the largest child presenting this type of heart, there being four infants larger than he. The measurements of the heart shadow did not show any constant relation to either the size of the baby or the size of the thorax. The position of the shadow also was not uniform and while it was usually more to the left than to the right (that is, the M. L. measurement was greater than the M. R. measurement) in two instances these two measurements were the same, and in another instance the M. R. was greater than the M. L.; the heart shadow being further over to the right of the median line.

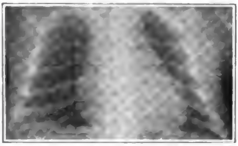

Figure 4

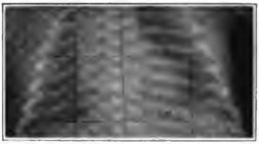

Figure 5

Fig. 4.—Serial No. 11. Radiograph No. 30457. Baby's weight, 8 pounds 6 ounces. Drop heart, typical, also largest. Heart negative. Thymus to left.

Fig. 5.—Serial No. 15. Radiograph No. 30456. Baby's weight, 9 pounds 3 ounces. Nutmeg heart, typical. Heart, negative. Thymus to right.

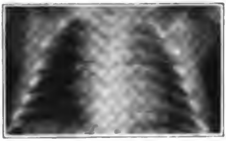

Figure 6

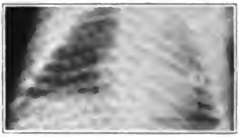

Figure 7

Fig. 6.—Serial No. 16. Radiograph No. 32668. Baby's weight, 6 pounds 13 ounces. Square heart, typical. Heart, negative. Thymus to right.

Fig. 7.—Serial No. 17. Radiograph No. 32669. Baby's weight, 6 pounds ½ ounce. Round heart, typical. Heart to left. Thymus negative.

The "adult" type also varied in size and position. The smallest heart of this type was found in one of the two smallest infants in this group of the same weight (5 pounds, 4 ounces), though it was in the one whose body measurements, height, weight, chest, abdomen were the larger of the two. Incidentally the thorax in this radiograph showed evidences suggestive of rickets. The largest shadow of this type was in the largest child of this group of seven. All of the shadows in this group were more to the left than to the right, though the positions varied considerably.

In the "drop" group, variations also occurred. The shadows in this group were more centrally located than in any of the other groups. In two of the five instances the M. R. was greater than the M. L. The smallest shadow in this group was present in the smallest infant of this group, and the largest shadow was seen in the largest infant.

In the "nutmeg" group there was apparently no relation between the size of the shadow and the size of the infant, and there was very little variation in the position of the shadow.

In the two instances in which the shadow was classified as "square" the interesting feature was the enormous area occupied by the shadow. In one instance the shadow was quite centrally located. In both instances the thymus was enlarged especially to the right.

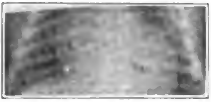

Fig. 8.—Serial No. 18, Radiograph No. 32088. Baby's weight, 9 pounds 12 ounces. Unusual heart. Heart shadow shows a heart markedly dilated to the right, its upper border apparently touches the side of the chest wall in the region of the fourth rib and blends down where the shadow merges with the diaphragm at the ninth rib in the midclavicular line. No way of differentiating thymus shadow.

The instance of the "round" shadow was found in an infant showing roentgenographic evidence in the ribs suggestive of rickets.

The "unusual" heart shadow showed a heart apparently markedly dilated to the right, its upper border seeming to touch the side of the chest wall in the region of the fourth rib and blend down where the shadow merges with the diaphragm at the ninth rib in the midclavicular line.

In the study of the shadow ascribed to the thymus, the following was noted: In connection with the globular hearts the thymic shadow was considered to be not enlarged in nine instances. In twelve instances the shadow was increased in size; in six, the increase was greater to the left side; in five, to the right, and in one equally to the right and left. In the six instances in which the thymic shadow was greater on the left side, in two instances each the heart shadow was increased to the left, increased to the right, and medially located. In the five instances in which the thymic shadow was increased to the right, the heart shadow was greater to the left in three instances, relatively greater to the right in one instance, and medially located in one instance.

In its relation to the "adult" type of heart the thymic shadow was increased in six instances, and not increased in one instance.

In five instances in which the heart shadow was greater to the left, the thymic shadow was increased to the left in two instances, and to both the right and left in three cases. In the two "adult" type hearts, centrally located, the thymic shadow was increased to the right in one instance and no enlargement was noticeable in the other.

In connection with the "drop" type of heart, in the five instances in which this type was recorded, the thymic shadow was not increased in one instance. In the four instances in which the thymic shadow was increased in size, of the two centrally located heart shadows, one was increased to the right and the other to the left. In the two remaining instances, the one in which the heart shadow was increased to the right the thymic shadow was also increased to the right; and in the other case in which the heart shadow was increased to the left, the thymic shadow was also increased to the left.

In its relation to the "nutmeg" variety of the heart the thymic shadow was increased in one of the three instances, the increase being greater to the right in association with a heart which was relatively greater to the right. The thymic shadow was negative in the other two instances of the "nutmeg" heart, in one case of which the heart shadow was much to the left, and in the other the heart shadow was relatively medially located.

The thymic shadow was enlarged in both instances of the "square" heart, in both of which it was increased to the right. There was no enlargement of the thymus in connection with the "round" heart which was centrally located. In the heart classified as "unusual" no thymic shadow could be differentiated.

We appreciate that conclusions cannot be drawn from the study of so few cases, but we believe that unless the way is opened for such a study and a start made information on this subject will not be forthcoming.

SUMMARY

The summary of our study may be enumerated as follows:

1. The heart shadows vary as to shape, size and position.
2. These variations occur with no relation to the size of the infant.
3. The heart shadows may be grouped in several types according to shape.
4. Variations in size and position occur in each of these types.
5. There is no constant relation between the heart shadow and the shadow of the thymus.

6. The shadow of the thymus is not necessarily influenced by the position of the heart.

7. The shadow of the thymus varies in its size and position independent of the heart shadow and with no relation to the size of the infant.

8. These variations in the shadows of the heart and the thymus can exist without clinical manifestations of disease.

GASTRIC MOTILITY AFTER PYLORIC OBSTRUCTION IN INFANCY *

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AND
R. WALTER MILLS
ST. LOUIS

In a ward discussion of pyloric stenosis and pylorospasm in infancy, the question was raised as to the results of operation or nonoperation upon gastric function and motility later on in life. Despite the voluminous literature on the subject of pyloric obstruction from both the medical and surgical standpoints, we were unable to find any data relating to this point, except the statement, which coincided with our own observation, that children who recovered from pyloric stenosis—either with or without operative intervention—seemed to develop normally and to have no ill effects from the early disorder and malnutrition.

In order to obtain some definite data we determined to hunt up some old medical and surgical cases which had been treated in the past at the St. Louis Children's Hospital and make studies of the gastrointestinal motility, and enlisted the services of Dr. Mills of the department of roentgenology to carry out the roentgen-ray examinations. The children were given a barium and milk meal in the morning on an empty stomach and the passage of the meal was watched with the fluoroscope. From time to time roentgenograms were made for permanent record.

It was decided to study two groups of cases—the nonoperated and the operated—for the purpose of comparison. After four cases in each group were studied we found the results were so uniform that it did not seem worth while to enlarge the series and we are presenting the findings in the eight cases in this paper.

REPORT OF CASES

Case 1 (47716).—*History*.—B. S., boy, 4 years of age, was first seen July 16, 1917, when 2 months of age. Weight at this time, 4,330 gm. The baby had been breast fed every three hours and when one month of age started to vomit shortly after feedings. The vomiting was projectile in type.

No tumor could be felt. Peristaltic waves were visible. The baby was watched for several days and a diagnosis of pylorospasm was made. As the nutrition was not bad, the baby was placed on atropin and lavage and kept on the breast. There was a slow but steady improvement and the vomiting gradually stopped after a period of several months. The baby was under

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* From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

observation for more than a year at an infant welfare center, but had not been seen for two years before the time it was brought back for examination.

Gastro-Intestinal Examination.—The barium meal passed rapidly and in a normal manner through the pylorus. Thirty-five minutes after the meal was given the clearance was active. A roentgenogram taken at four and three-quarters hours (Fig. 1) shows a small amount left in the stomach, but nearly all of the meal in the small intestine, cecum and ascending colon. The conditions as to gastric motility are considered as normal.

Case 2 (45221).—*History.*—C. B., boy, 4⅓ years of age, came under observation in April, 1917, when 5 months of age. At this time the baby was badly undernourished, weighing 3,900 gm. He had been fed for two months on the breast and since that time on various milk modifications and proprietary foods in an attempt to check the persistent vomiting which had been present since the second or third week of life. The baby had typical projectile vomiting.

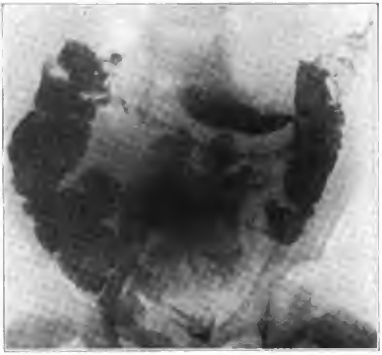

Fig. 1.—Case 1 (no operation), four and three-quarters hours after meal. Small amount still in stomach.

No tumor mass could be felt. Peristaltic waves were present. A diagnosis of pylorospasm was made and atropin (1/600 grain) before each feeding was started. The vomiting gradually became less and the general condition of the patient improved slowly but steadily. The baby was kept under observation and treatment for some time.

Gastro-Intestinal Examination.—Under the fluoroscope the barium and malted milk was observed to pass normally through the stomach. Figure 2, taken immediately after the meal had been given, shows the barium already passing through the pylorus, and Figure 3, taken four and one quarter hours later, shows the stomach empty.

Case 3 (6038).—*History.*—V. S., boy, 8 years of age was treated in the hospital in November and December, 1913. He was brought to the hospital when 10 weeks of age, weighing 5½ pounds. He was said to have weighed 7½ pounds at birth and then gained about two pounds. Near the end of the first month he started to vomit. The vomiting increased steadily and there was a loss of weight. In the hospital it was noted that visible peristalsis, accompanied by projectile vomiting, following each feeding.

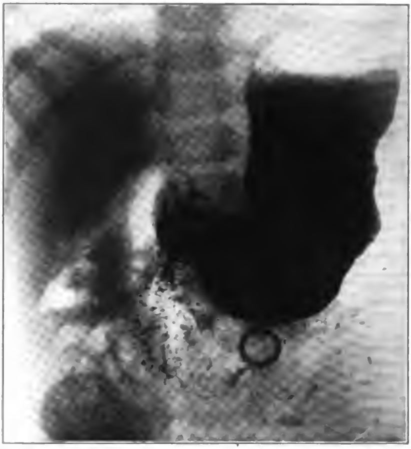

Fig. 2.—Case 2 (no operation), shortly after meal. Shows barium passing through pylorus.

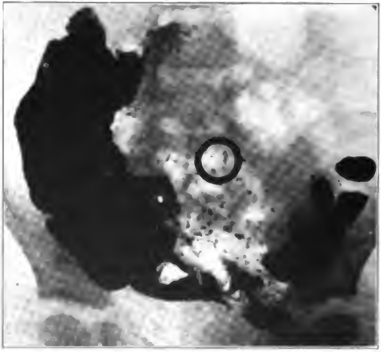

Fig. 3.—Case 2 (no operation), four hours after meal. Stomach empty and barium in small intestine and colon.

No tumor was palpable. A diagnosis of pylorospasm or pyloric stenosis was made and lavage, together with atropin, before each breast feeding was started. There was gradual, slow and rather irregular improvement, vomiting decreasing and increasing again in turn. After seven weeks of hospital treatment, the baby was cared for in the Outpatient Department. After six months the vomiting stopped and by ten months the baby had reached the normal weight line.

Gastro-Intestinal Examination.—In this case the conditions as to gastric motility were likewise found normal. There was no abnormality in the initial motility and the pylorus was definitely canalized, actively and passively. If anything, the motility must be considered very active, as four hours after the meal was taken the stomach was empty and the barium was in the colon.

Case 4.—*History.*—C. B., girl, 6½ years of age, was a sister of the patient in Case 5. This baby was not treated by us when an infant, but was treated for pyloric stenosis at her home and at another hospital. The history was typical of the condition. The baby was attended by two excellent pediatricians and there is no question as to the diagnosis. She was not operated on, but was treated with lavage and atropin. Two years later another child (Case 5) was born and when 4 weeks of age he developed the same condition. This second baby came into the hospital and was operated on, as reported later. The father very kindly consented to the examination of both children. The nonoperated baby had a very difficult first year. She has never been a strong and healthy child and has about the same physical development as the brother, who is two years younger and who was operated on. This is the only case in our experience in which we have evidence that the malnutrition in infancy, which was severe in this case, seemingly affected the development of the child.

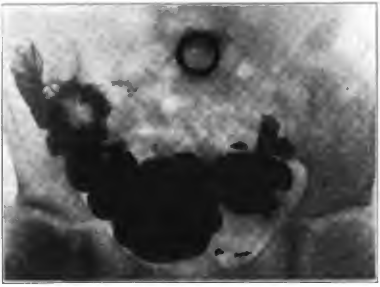

Fig. 4.—Case 4 (no operation), four and one quarter hours after meal. Stomach empty and barium almost entirely in colon.

Gastro-Intestinal Examination.—Normal conditions were found as to gastric motility and gastric structural conditions. There was a slight initial pyloric spasm lasting for ten minutes observed under the fluoroscope, but no apparent abnormality in the length or width of the pyloric sphincter. There was no suggestion of gastric dilatation or other abnormality. The duodenal cap and pylorus were perfect in formation. Figure 4, at four and one fourth hours, shows the stomach empty and the barium meal in the small intestine, cecum and ascending colon.

Case 5 (11194).—*History*.—C. B., a boy, aged 4½ years, is the brother of the patient in Case 4. He was breast fed. When 4 weeks of age he developed typical pyloric obstruction with projectile vomiting, starvation stools and visible peristalsis. He was sent to the hospital and failed to improve on routine medical treatment. He was then operated on by Dr. Clopton, who found a thick, olive shaped pyloric tumor with a greatly enlarged stomach. The muscle was incised by the Rammstedt method and measured 7 mm. in thickness. The vomiting stopped after the operation and the child made a good recovery and gained weight rapidly.

Gastro-Intestinal Examination.—Normal conditions were found as to gastric motility and structural conditions. There was no suggestion of gastric dilatation or other abnormality. The pylorus and cap formation were perfect, and under the fluoroscope no abnormality in the length or width of the pyloric sphincter was found. At the end of four and a half hours there was a very slight amount of the barium meal left in the stomach, but nearly all had passed into the small intestine, cecum and ascending colon.

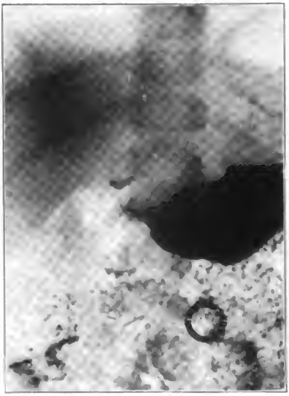

Fig. 5.—Case 7 (operation), shortly after meal. Barium passing through pylorus.

Case 6 (15188).—*History*.—J. T., male, 15 months of age, was admitted to the hospital in February, 1920, when one month of age. Birth was normal. When about two weeks old, the baby started to vomit and nearly all of the feedings were regurgitated. On examination visible peristalsis and a palpable tumor were found. The baby failed to respond to medical treatment and ten days after admission was operated on. A moderate size tumor was found which was incised according to the Rammstedt method. The baby stopped vomiting the day following the operation and did not vomit again while in the hospital. The baby started to gain weight rapidly and at the end of the first year the weight was normal. This baby has been under constant observation and has never shown the slightest abnormality in gastric function since the operation.

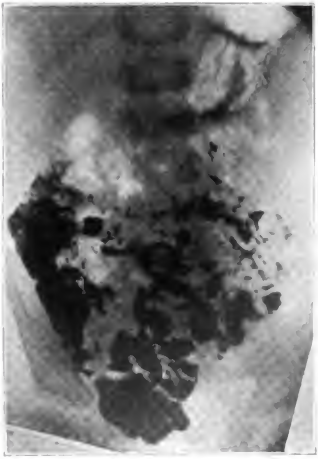

Fig. 6.—Case 7 (operation), four hours after meal. Stomach empty.

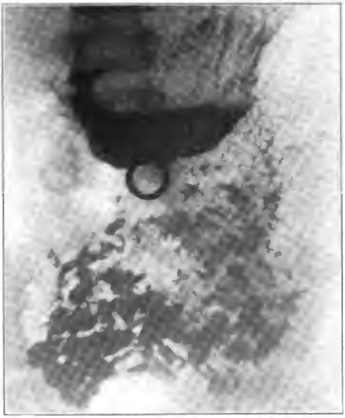

Fig. 7.—Case 8 (operation), shortly after meal. Shows barium passing through pylorus.

Gastric-Intestinal Examination.—On roentgen-ray examination there was no apparent abnormality in the motility with the possible exception of a slight retardation in total motility, as at the end of four and three fourths hours a moderate amount of the barium meal was still in the stomach. The initial motility was normal and the pylorus was definitely canalized. No abnormality was apparent in the width of the pyloric sphincter.

Case 7 (11416).—*History.*—A. S., girl, 4 years of age, was admitted to the hospital in April, 1917, when 5 weeks of age. She had been breast fed for three weeks. One week after birth vomiting was said to have started. Because of the vomiting the food was changed to an artificial mixture. When brought to the hospital the baby was in bad condition, weighing 3,450 gm. Vomiting was projectile in type; peristaltic waves were present and a tumor mass palpable. Because of the malnutrition, the baby was operated on the day following admission and a large pyloric tumor was found, measuring 1.5 cm. in diameter. The stomach was markedly distended. Vomiting stopped following operation and the baby's condition gradually improved until in a few months the condition of nutrition was normal.

Gastro-Intestinal Examination.—The pylorus was observed to function normally under the fluoroscope, canalization taking place, cap and pyloric formation being perfect. Four hours after the meal was taken, the stomach was practically empty and the barium had passed into the small intestine, cecum and ascending colon. Two pictures of this case are shown, Figure 5, taken shortly after meal was given and showing the pylorus; and another, Figure 6, taken four hours later, showing the meal in the small intestine. Conditions as to gastric motility are considered normal.

Case 8 (9615).—*History.*—Z. B., boy, 5 years of age, was admitted to the hospital in December, 1915, when 2 months of age. When 3 weeks of age the baby started to vomit and this continued until time of admission. When brought to the hospital the baby was very badly nourished, weighing 3,600 gm., peristaltic waves were present and stools were of the starvation type, but no tumor could be felt. The child was treated medically for three weeks. At first it started to improve, but then started to lose weight and so three weeks after admission was operated on. A typical hard cartilaginous tumor was found, 2 cm. in diameter. This was incised. Following the operation vomiting decreased gradually and in about two weeks the baby started to gain. The child was followed through the outpatient department and in a few months all signs of malnutrition had disappeared.

Gastro-Intestinal Examination.—Under the fluoroscope the pylorus was found to function normally. The pyloric sphincter did not appear thicker than normal and the cap and pyloric formation was perfect. The total gastric motility was normal, the stomach being empty after four hours. Figure 7 was taken shortly after the meal was given and gives a very clear picture of the barium meal passing through the pylorus and a small amount in the small intestine.

DISCUSSION

The gastric motility of eight children, all of whom had been patients with pyloric obstruction in early infancy, was studied and in every instance was found normal. Four of these, aged 4, 4⅓, 6 and 8 years, respectively, had been treated medically, and in four cases, aged 1⅓, 4, 4½ and 5 years, respectively, a pyloroplasty (Rammstedt operation) had been done. In the latter four cases a definite tumor was found, but as to whether the obstruction was due to tumor or simple spasm in the four medically treated cases is, of course, uncertain and therefore we have classified them as pylorospasm. In each one of these cases persistent vomiting of a projectile type, small stools, visible peristalsis, and malnutrition were present.

At the time of the gastric examination the children were all in a good condition of nutrition and with one exception (Case 4) they had developed normally after overcoming the trouble in early infancy. All belonged to the "sthenic" type of habitus, as classified by Mills.[1]

There is little data in regard to gastric motility in children. In the "sthenic" type of habitus in adults the stomach usually empties in from four to five hours, the average time in round numbers in this type, as determined by Mills[2] in a series of 481 cases, being four hours and forty-five minutes. Interestingly, in asthenic adults complete gastric motility was found by the same author definitely slower, the average time of such total emptying being five hours and forty-five minutes in 118 cases. It would be very interesting if comparable figures of the time of complete gastric motility in different types of children were available. Figures of this sort are a necessity if such time varies anything like what it does in adults. In adults, as determined by Mills, the intermediate hyposthenic type of habitus has a total motility of five hours and thirty minutes as found in a series of 354 subjects and the extreme hypersthenic type, persons of massive physique, high stomachs, and rapid general alimentary motility, has the most rapid gastric motility, four hours and fifteen minutes in a series of forty-seven cases. A factor also to be taken into consideration in studies of complete gastric motility in different types, certainly in adults and also in children by inference, is the incidence of the various types of physique. If one or two intermediate types are, as is actually the case, numerically in marked preponderance as are the sthenic and hyposthenic, the time of complete gastric motility in these types should be considered the average or "normal" time, and those of the less frequently occurring hypersthenic and asthenic types as exceptions; yet whose motility time is to be judged by that of similar persons. Figures as to the incidence of types also compiled by Mills from observations on 1,000 adults without known organic or marked functional disturbances are as follows: Hypersthenic habitus, forty-seven, 4.7 per cent.; sthenic habitus, 481, 48.1 per cent.; hyposthenic habitus, 354, 35.4 per cent., and asthenic habitus, 118, 11.8 per cent.[3] Recently Sauer, Minsk and Alexander[4] reported considerable slowing of the gastric motility in children with anorexia, and for comparison cite the cases of twelve children with good appetite of the "sthenic" habitus. In these children the stomach was empty in one instance by three and one-half hours; in four by four hours; in two by four and one-half hours, and in the remaining five by five hours. In five of our cases the stomach was empty by four and one-half hours or less and in the remaining three cases only a very slight amount was left by this time. Our figures, therefore, fall well within the limits of what may be considered as normal gastric motility. In children of hyposthenic or asthenic habitus the stomach frequently is not emptied before six or seven hours after the meal is given.

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[1] Mills, R. W.: Am. J. Roentgenology **4**:155 (April) 1917.

[2] Mills, R. W.: Tr. Am. Gastro-enterological Assoc. **36**:47, 1918.

[3] As an aside, the variation in the incidence of different types of habitus should be taken into consideration in many other conditions, such as the relative occurrence of different diseases in different types; for example, tuberculosis, as occurring in asthenics. Since the asthenic type is comparatively rare, tuberculosis is very much more predilected in such type than is apparent at first sight.

[4] Sauer, Minsk and Alexander: J. A. M. A. **79**:184 (July 19) 1922.

It was of particular interest to find that there was no difference between the cases of pyloric obstruction treated medically and those treated surgically. This was the original point raised and our findings lead us to conclude that the late or end-results cannot be taken into consideration in a given case of pyloric obstruction in infancy, in deciding for or against operation.

CONCLUSIONS

The gastric motility was studied in eight children from 1½ to 8 years of age, who had been treated for pyloric obstruction in early infancy. Four had been treated medically and four surgically (Rammstedt operation). In every instance conditions as to gastric motility were found normal.

THE RATE OF SECRETION OF BREAST MILK*

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AND
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The problems involved in breast feeding have been studied long and exhaustively and there remains little to be said on the subject. There is one point, however, on which medical writers are indefinite, that is, the length of time which a baby should be allowed to stay at the breast at each feeding.

Twenty minutes at each nursing is usually taught as an absolute rule to nurses and physicians, and by them transmitted to the mother. This tradition has been handed down from generation to generation and is seldom questioned.

Few textbooks mention definitely the nursing time, merely stating that it should not be prolonged beyond 20 minutes, and that often from ten to fifteen minutes will suffice. Many authors state that the baby may nurse until satisfied or sleepy. A few hint at what we have found to be the real facts, but are not sufficiently definite.

Still says, "The time taken at the breast should be about 15 minutes. Some infants suck so rapidly that they will empty breasts in less than ten minutes, with resulting colic and vomiting. To prevent this mothers should regulate the flow by compressing the nipple with the hand."

It seems to us that the colic and vomiting described may more properly be attributed to overfeeding than to rapid feeding.

Kerley says, "Weighing the baby at intervals of from three to five minutes and noting gain has shown that from three to four ounces, which may represent the child's stomach capacity, may be obtained in two, three or five minutes. From a free, full breast a good nurser will take one ounce in one minute. The idea that a nursing infant will take no more than is good for him is the fruit of inexperience."

Grulee says, "As an arbitrary rule it is not well to leave the baby at the breast longer than from fifteen to twenty minutes. In restricting the time at the breast we must take in consideration that in the first five minutes the child gets as much as in the next ten minutes."

This study was undertaken to try to ascertain the facts in this matter. The objects in mind were: (1) to determine the rate at which the baby gets the milk from the breast; (2) to determine the average time which is taken to obtain the entire feeding.

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* Received for publication June 20, 1922.

* From the Children's Medical Division, Bellevue Hospital, and the Department of Diseases of Children, Columbia University.

* Read before the American Pediatric Society, May 1, 1922.

In order to ascertain these points we have used the method of "fractional weighing," that is, weighing a number of babies at frequent intervals during nursing. The increase in weight during each interval represents the milk secreted. By using a scale which weighs accurately to ¼ ounces quite correct figures are obtained.

It may fairly be said, it seems to us, that it is not desirable to let a baby nurse after he really stops getting milk from the breast. The child who sucks will swallow, and if there is no milk he will swallow air. This increases his gastric distension and predisposes to vomiting and colic, as was pointed out by Smith and LeWald[1] several years ago.

Prolonged nursing is bad for the baby also because it means fostering the habit of chewing the nipple when no milk is being secreted.

In the second place, the saving of the mother's time is important. The following examples show what this may mean:

A mother had two babies eleven years apart. During the early months the first was nursed twenty minutes every two hours, or 200 minutes a day. The second was nursed five minutes every four hours, or twenty-five minutes a day. The mother saved 175 minutes or nearly three hours of her time a day, and the second baby did perfectly well.

Another mother nursed her first child twenty minutes every two hours, nine feedings, or 180 minutes a day. At ten weeks the child developed eczema, was cut down to forty seconds every four hours, five feedings, or 200 seconds a day, about one-sixtieth of the first plan. This mother had such an abundant and rapid milk secretion that the baby still gained on the very short nursing periods.

In addition, the sparing of the mother's nervous system has to be considered. A great many women complain that the prolongation of the nursing to fifteen or twenty minutes makes them exceedingly nervous, while they do not mind short nursings at all.

It is also bad for the nipple to have the baby chew on it longer than is necessary.[2]

The point may be raised that the supply of breast milk is more likely to fail if the nursings are shortened too much. This point has been carefully noted by one of us for several years, and breast milk does not seem to fail more quicky on relatively short nursings than it did on the older principle of prolonged ones.

Another possible objection may be that it has been found by analysis that the breast milk taken at the latter part of the nursing (strippings)

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1. Smith, C. H., and LeWald, L. T.: The Influence of Posture on Digestion in Infancy, Am. J. Dis. Child. **9**:261 (April) 1915.

2. In discussing this paper, Dr. R. S. Haynes said that the incidence of cracked nipples had been much reduced at The Sloane Maternity Hospital since the nursing time had been cut down from twenty minutes to eight or ten minutes.

is richest in fat, and that, therefore, he child's nursing time should not be reduced lest he lose this necessary part of the milk. This is doubtless true, but does not excuse leaving the baby at a breast which has been emptied, and from which he is getting no milk whatever.

The method of "fractional weighing" used in this study is not a new one, since it has long been used as a routine by many clinicians for determining the length of time a baby should be allowed to nurse, and for deciding whether he needs one breast or both for each feeding.

We have used the two minute interval in the majority of the cases studied. Some observations have been made at one minute intervals, but this gives too short a time between the weighings for the baby to get a good start. The time has been taken from the instant nursing began, and the baby has been removed from the breast promptly at the end of two minutes whether he has nursed vigorously or fitfully. Few of the babies object to being interrupted for the few seconds which it takes to weigh them. The nursings have been continued on one breast until the baby obtained nothing during one or two periods of two minutes, or until he refused to nurse any more; a few were stopped when vomiting occurred. In most cases the baby was offered the second breast, and allowed to nurse until the weight remained stationary or until the baby refused to continue.

It is obvious that there are many factors which must be considered in studying the results obtained, such as the age of the baby, his weight, whether he is of average size, overweight or underweight; his vigor and his temperament. Furthermore, the time of day is of no small importance. The morning nursings give a larger amount than those taken in the afternoon, as a rule. A great many of our observations were made in the out-patient department between 2 and 5 o'clock, when the milk supply is not at its best.

The condition of the breast, its size and fullness, the variation between the two sides, and whether one breast or both are necessary, all bear directly upon the figures obtained. If the infant is thriving and the supply of milk bids fair to continue, we must interpret a single poor nursing in a different light from a similar one obtained from a definitely failing breast. The matter of added bottles also make some difference in the manner in which baby does his share of the nursing. If the breast milk is growing scanty the baby will often refuse to nurse well, preferring to wait for the bottle which he has learned to expect.

We find that our observations fall naturally into four groups according to the amount obtained in relation to the wight of the child. It is not possible to compare the nursing curve of a large child who gets 6 or 7 ounces from one breast with that of a 6 pound baby who gets only ½ ounce from two breasts.

We have assumed that a good feeding is one in which a baby gets about 0.4 ounce (or more) per pound of body weight.[3] But since we are dealing with breast milk a somewhat smaller amount, 0.33 ounces per pound, has been assumed to be adequate.

The observations have been grouped as follows:

1. Adequate feeding from one breast (more than 0.33 ounce milk per pound). Twenty per cent. of our observations fall into this class.
2. Adequate feedings from both breasts. Twenty-five per cent. are in this class.
3. Fair feedings from the two breasts (from 0.25 to 0.33 ounce of milk per pound). These babies were mostly fed on the breast alone and were doing well; the comparatively poor nursing was probably only due to the time of day or other factors. Twenty per cent. are in this class.
4. Poor feedings. These babies obtained less than 0.25 ounce of milk per pound from two breasts. They make up 35 per cent. of the observations. This group contained the largest number of babies who were given bottle or cereal in addition to the breast (fifteen of the thirty-five). The milk supply was failing in a good many cases.

A mass of figures like these can be best studied by the graph method. We have plotted all our observations separately—but have shown only a few typical feedings (Fig. 4) and the curves of averages (Figs. 1, 2 and 3) of the various groups. Each average curve has been continued as long as any individual baby obtained milk. This does not mean that all the group got milk to the point represented by the end of the curve. The average time after which no more milk was obtained ("average emptying time" of the breast) is plotted on each line as a circle surrounding a dot.

In studying the curves in each group, it is necessary again to subdivide according to the size of the baby. We have taken weight as the criterion rather than age. As a matter of fact, this is a fair thing to do because more of the babies have been over weight for their age rather than under. We have divided them into: (1) those under 9 pounds; (2) those from 9 to 12 pounds; (3) those from 12 to 15 pounds, and (4) those over 15 pounds.

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[3] This amount was derived from the following: In the early months the child needs 3 ounces of fluid per pound of body weight (one-fifth of his weight) and seven feedings: $\frac{\text{Wt.} \times 3}{7} = 0.4$ In the middle months the child needs 2½ ounces per pound (from one-sixteenth to one-seventeenth of his weight) and from five to six feedings. $\frac{\text{Wt.} \times 2\frac{1}{2}}{6} = 0.4+$. In the latter months he will take 2 ounces per pound (one-eighth of his weight) and five feedings $\frac{\text{Wt.} \times 2}{5} = 0.4$. Therefore, 0.4 ounce of fluid per pound is about the amount needed for all babies.

This gives three or four curves on each chart, one for each group of babies by weight. Some of them contain only a few observations, but the individual variations from the average are not great.

The twenty observations in which the baby obtained an adequate feeding from one breast (Table 1 and Fig. 1) were made on sixteen different babies. All but three were being fed on breast alone.

The curves (Fig. 1) show a distinct similarity—a rapid rise in the first three periods, followed by a very small gain in each succeeding one. In all three the baby obtained about 40 per cent of the total amount in the first two minutes; from 60 to 70 per cent. in the first four minutes; from 75 to 85 per cent. in the first six minutes

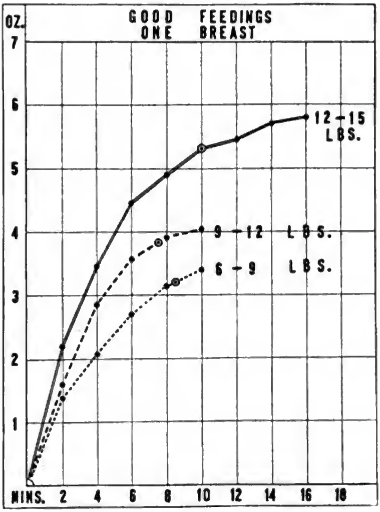

Fig. 1.—Curves obtained by averaging observations in Table 1, grouped according to the weight of the babies. Each curve is continued as long as any baby obtained milk. Average time after which no more milk was obtained is shown by circle surrounding dot.

The average emptying time is shown as 8.5 and 7.6 minutes, respectively, in the two lower curves. None of the babies obtained any milk after ten minutes. Of the larger infants (from 12 to 15 pounds) one obtained some milk up to fourteen minutes and one up

TABLE 1.—GOOD FEEDINGS SINGLE BREAST

Observation Number	Bottle	Cereal	Weight, Pounds	Age	Ounces of Milk Obtained in Each 2 Minute Period								Total, Oz.	Ounces Milk per Pound
					2	4	6	8	10	12	14	16		
1	..	..	6¼	7 weeks	0.5	0.5	0.75	0.75	0	....	....	....	2.5	0.4
2	+	..	6½	7 weeks	1.75	0.75	0.5	0.25	0.25	0	....	....	3.5	0.56
3	..	..	7	1 month	2	0.75	0.25	Ref.	....	....	....	....	3	0.43
4	+	..	8	3 weeks	1.25	0.76	1	0.75	0.25	Ref.	....	....	4	0.5
5	..	..	9¾	1 month	1.75	1	0.75	0.25	0	0	....	....	3.75	0.375
6	..	..	9¾	2 weeks	2.5	1	0.25	Ref.	....	....	....	....	3.75	0.375
7	..	..	10¼	6 weeks	2	1	0.5	Ref.	....	....	....	....	3.5	0.35
8	..	..	10¼	6 weeks	2	1.5	0.5	Ref.	....	....	....	....	4	0.4
9	..	..	10¼	3 weeks	1	1.5	0.5	1	Ref.	....	....	....	4	0.4
10	..	..	10½	6 weeks	1	1	1.5	0.5	1.25	Ref.	....	....	5.25	0.48
11	..	..	11	8 weeks	0.5	1	1	1	0.5	0	....	....	4	0.37
12	..	..	10¾	6 weeks	2	1.5	0.5	0.5	St.	....	....	....	4.5	0.41
13	..	..	10¾	6 weeks	2	1.5	0.5	Ref.	....	....	....	....	4	0.37
14	..	..	11¾	2½ months	1.25	1.5	1.25	1	Ref.	....	....	....	5	0.42
15	..	..	12¾	2 months	2	1.25	1	Ref.	....	....	....	....	4.25	0.34
16	..	..	13	2½ months	0.5	1.75	1	0.25	0.25	0.5	0.75	0.5 R.	5.5	0.42
17	..	..	13¾	4 weeks	2	1.75	2.5	1	Ref.	....	....	....	7.25	0.53
18	+	..	14½	7 months	3.5	1	0	0:5	1.25	0	....	....	6.25	0.43
19	..	..	15	5 months	3	1	1	0	....	....	....	....	5	0.34
20	..	..	15¼	3 months	2.25	0.75	0.5	1	1	0.25	0.75	0	7	0.46

to sixteen minutes, which prolongs this particular curve and makes the average emptying time ten minutes. Two of these children, however, emptied the breast in six minutes. Most of these babies are under two months old, and all but two weighed less than 15 pounds.

Figure 2 shows the nursings which were adequate from two breasts. In three of the groups from 58 to 68 per cent. was obtained from the first breast. In one group (from 9 to 12 pounds) about 50 per cent. came from each side. The smaller nursing from the second breast, is probably due to the fact that the baby loses the first edge of his appetite after he has obtained some food.

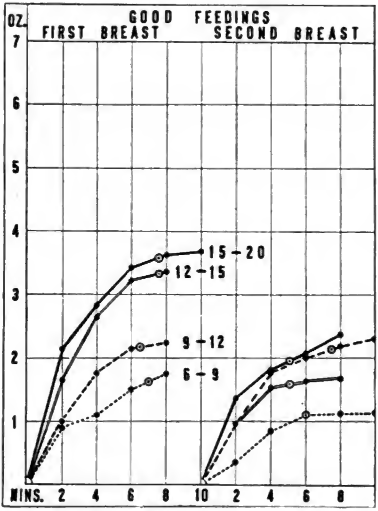

Fig. 2.—Curves showing average of observations from Table 2. Curves representing average amounts from second breast are plotted in broken, double, or solid lines to correspond to those of first breast. Average emptying time shown by circle and dot.

The secretion in the individual breasts follows the general rule. Most of the milk is obtained in the first four minutes (from 65 to 80 per cent.) and the largest amount in a single period is in the first two minutes (from 45 to 58 per cent.). The average emptying time is from 6½ to 7½ minutes.

TABLE 2.—GOOD FEEDINGS BOTH BREASTS

Observation Number	Bottle	Cereal	Weight, Pounds	Age	Ounces of Milk Obtained in Each 2 Minute Period						Total First Breast	Ounces of Milk Obtained in Each 2 Minute Period						Total Second Breast	Total Both Breasts	Ounces Milk per Pound
					2	4	6	8	10	12		2	4	6	8	10	12			
21	+	..	6¾	3 wk.	0.5	0.25	0.25	0.5	0	....	1.5	0.5	0.25	0	0.25	0.25	0	1.25	2.75	0.4
22	..	..	7½	1 mo.	1.75	0	0	....	....	....	1.75	0.25	0.5	1	0	....	....	1.75	3.5	0.46
23	..	..	7½	5 mo.	0.5	0.25	0.25	0.25	0	....	1.25	0.5	0.5	0.25	V.	....	....	1.25	2.5	0.34
24	..	..	8	3 wk.	0.75	0.25	0.5	0.25	0	....	1.75	0.75	0.5	0	....	....	....	1.25	3	0.375
25	..	..	8	1 mo.	1	0.25	0.5	0.25	Ref.	....	2	0	0.75	Ref.	....	....	....	0.75	2.75	0.34
26	..	..	9¾	2 mo.	1.25	1	0	0.5	0	0	2.75	0.75	1	0	0.5	0	....	2.25	5	0.5
27	..	..	9¼	1½ mo.	0.5	0	0.25	0.25	0	....	1	0.5	1	0.25	0	0.5	0	2.25	3.25	0.38
28	+	..	9¼	6 wk.	1	0.25	0.5	0	....	....	1.75	0.25	0.5	0.5	0.5	0	....	1.75	3.5	0.4
29	..	..	10	2½ mo.	1.25	0.5	0.25	0	....	....	2	1	0.75	Ref.	....	....	....	1.75	3.75	0.38
30	..	..	10	11 wk.	1	1.5	0	....	....	....	2.5	1.5	1.5	0.5	Ref.	....	....	3.5	6	0.6
31	..	..	10¾	3½ mo.	0.75	0.75	0.5	0	....	....	2	0.75	0.5	0.5	0.25	0.25	Ref.	2.25	4.25	0.4
32	+	..	11	5 mo.	1	1.5	0.5	0	....	....	3	1.5	0.5	0	0	....	....	2	5	0.45
33	..	..	11¾	2½ mo.	1.25	0.5	0.25	0	....	....	2	1.25	1.25	1	0.25	0.5	0	4.25	6.25	0.54
34	..	..	12	3 mo.	1.25	0.75	0.5	0.25	0.5	0	3.25	0.75	0.25	0.25	0.25	V.	....	1.5	4.75	0.4
35	..	..	13¼	3½ mo.	1	1.5	0	....	....	....	2.5	1	1.25	0	....	....	....	2.25	4.75	0.36
36	..	..	13¼	3 mo.	1.75	1.25	0.75	0	....	....	3.75	0.5	0.5	0.25	0	....	....	1.25	5	0.385
37	..	..	13¾	4 mo.	1	0.75	0.5	0.25	0	....	2.5	1.25	1.25	0	....	....	....	2.5	5	0.37
38	..	..	13¼	3 mo.	2	1.75	0	....	....	....	3.75	1	0	....	....	....	....	1	4.75	0.35
39	..	..	14½	5 mo.	3.5	0	1	0	....	....	4.5	2	1	0.5	St.	....	....	3.5	8	0.55
40	..	..	14¾	3 mo.	2	1.25	0.5	0.5	0	....	4.25	0.25	0.25	0	....	....	....	0.5	4.75	0.33
41	+	..	15½	4½ mo.	2	1	0.5	0	....	....	3.5	1	0.75	0	....	....	....	1.75	5.25	0.34
42	..	..	15½	3 mo.	1.75	0.25	0.5	0.25	0	1.25	4	0.5	0.75	0.25	0.5	0	0	2	6	0.4
43	..	..	16¾	5 mo.	1.5	0 5	1.25	0.75	0.25	0	4.25	2	0	....	....	....	....	2	6.25	0.37
44	..	+	18¼	7 mo.	3.5	1.75	0.75	0	....	....	6	0.75	0.75	0	....	....	....	1.5	7.5	0.4
45	+	..	19¾	6 mo.	2	1	0	....	....	....	3	2.5	0	0.75	1	0	....	4.25	7.25	0.37

From the second breast again from 70 to 80 per cent. was obtained in the first four minutes. The variation of individual nursings is from two minutes to ten minutes. Most of the babies had emptied the breast in from six to eight minutes. The average time is from five to seven and one half minutes. These babies who needed two breasts are, in general, somewhat older than the first group.

The fair nursings (Table 3 and Fig. 3) include twenty observations on babies, 60 per cent. of whom were being fed on breast alone and were doing well. The curves of the first breast show a similar form to the good nursings except that they are shorter, nearly all having finished at six minutes. The average emptying time (four, four and eight-tenths and five and three-tenths minutes) is short except in one group, (seven minutes).

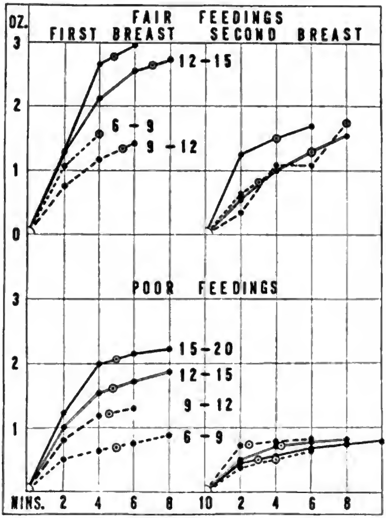

Fig. 3.—Curves showing averages of observations from Tables 3 and 4. Same conventions as Figures 1 and 2.

The second breast curves are somewhat more irregular but are based on only a few nursings, since several of these babies refused the second breast. The emptying time is short in most cases.

TABLE 3.—FAIR FEEDINGS BOTH BREASTS

Observation Number	Bottle	Cereal	Weight, Pounds	Age	Ounces of Milk Obtained in Each 2 Minute Period						Total First Breast	Ounces of Milk Obtained in Each 2 Minute Period						Total Second Breast	Total Both Breasts	Ounces Milk per Pound
					2	4	6	8	10	12		2	4	6	8	10	12			
46	+	..	8	3 wk.	0.75	0.25	0	....	....	....	1	0.75	0.75	0	....	....	....	1.5	2.5	0.31
47	..	..	8½	3 wk.	1.5	0.75	0	....	....	....	2.25	0.5	0	....	....	....	....	0.5	2.75	0.32
48	..	..	10	1 mo.	0.75	0.75	0.5	0	....	....	2	0	0.5	0	0.75	0	....	1.25	3.25	0.325
49	+	..	10½	2 mo.	0.75	0.5	0	....	....	....	1.25	0.25	0.75	0	0.5	0	....	1.5	2.75	0.26
50	..	..	11¾	2 mo.	0.75	0	0.25	0	....	....	1	0.75	1	0	0.75	Ref.	....	2.5	3.5	0.30
51	..	..	12	3 mo.	1	0.5	0.5	0.5	0.5	Ref.	3	Ref.	....	....	....	....	....	Ref.	3	0.25
52	..	..	12½	2½ mo.	1.25	1	0.25	0.25	0	....	2.75	0.25	0.25	0	....	....	....	0.5	3.25	0.27
53	..	..	12¼	3¼ mo.	1	1.25	1.25	Ref.	....	....	3.5	Ref.	....	....	....	....	....	Ref.	3.5	0.28
54	..	..	12½	2½ mo.	0	0.5	0.25	0.25	0	0	1	0.75	0.5	0.75	0.5	0	0	2.5	3.5	0.28
55	+	..	12¾	5½ mo.	1	0.5	0.5	0.25	St.	....	2.25	1	0.75	0	0.5	St.	....	2.25	4.5	0.35
56	+	..	13	8 mo.	2	1.5	0.25	0	....	....	3.75	Ref.	....	....	....	....	....	Ref.	3.75	0.29
57	..	..	13½	3½ mo.	2	1.25	0	....	....	....	3.25	0	....	....	....	....	....	0	3.25	0.25
58	..	..	13½	4 mo.	1	0.75	0.75	0.75	....	....	3.25	0.25	0	....	....	....	....	0.25	3.5	0.27
59	..	..	13¾	3 mo.	0.75	1	0	....	....	....	1.75	0.5	0.75	0.75	0.25	0	....	2.25	4	0.30
60	..	+	14	7 mo.	2.75	0.25	0.5	0.25	Ref.	....	3.75	0	....	....	....	....	....	0	3.75	0.27
61	+	..	15	4 mo.	1.75	0.5	0	....	....	....	2.25	1.5	0	....	....	....	....	1.5	3.75	0.25
62	+	..	15	4 mo.	1.5	1	0	....	....	....	2.5	1.5	0.5	0	....	....	....	2	4.5	0.3
63	+	..	15½	5 mo.	1.5	2	0	....	....	....	3.5	1.25	0.25	0.25	0	....	....	1.75	5.25	0.34
64	+	..	16	7 mo.	1	2	1	0	....	....	4	1	0	0	....	....	....	1	5	0.31
65	..	..	18	8½ mo.	0.75	1.25	0.5	0	....	....	2.5	1	0.5	0.75	0	....	....	2.25	4.75	0.26

TABLE 4.—POOR FEEDINGS BOTH BREASTS

Observation Number	Bottle	Cereal	Weight, Pounds	Age	Ounces of Milk Obtained in Each 2 Minute Period						Total First Breast	Ounces of Milk Obtained in Each 2 Minute Period						Total Second Breast	Total Both Breasts	Ounces Milk per Pound
					2	4	6	8	10	12		2	4	6	8	10	12			
66	+	..	8¼	1 mo.	0.75	0	0	....	....	....	0.75	0.25	0.25	0.25	....	....	....	0.75	1.5	0.19
67	..	..	8¼	1 wk.	0.25	0.25	0.25	0.25	0	0	1	0.5	0	0	....	....	....	0.5	1.5	0.18
68	+	..	9¼	2 mo.	0.75	0.25	Ref.	....	....	....	1	0.5	0	....	....	....	....	0.5	1.5	0.17
69	..	..	9½	1 mo.	0.5	0	....	....	....	....	0.5	1.25	0	....	....	....	....	1.25	1.75	0.18
70	..	..	9¾	6 wk.	0.75	0.5	0.5	0	....	....	1.75	0.5	0	....	....	....	....	0.5	2.25	0.23
71	+	..	10¼	2 mo.	0.75	0.25	0.25	0	....	....	1.25	0.5	0	....	....	....	....	0.5	1.75	0.17
72	..	..	10¾	1 mo.	0.5	0.25	0.25	0	....	....	1	1.5	0	....	....	....	....	1.5	2.5	0.23
73	..	..	10¾	2½ mo.	1.25	0.25	0	....	....	....	1.5	0.5	0.5	Ref.	....	....	....	1	2.5	0.23
74	..	..	11¾	2 mo.	0.5	0.25	0	....	....	....	0.75	0.75	Ref.	....	....	....	....	0.75	1.5	0.13
75	..	..	11¼	2 mo.	1	0.75	0.25	0	....	....	2	0.25	0	0 .25	0	....	....	0.5	2.5	0.225
76	..	..	11¾	4 mo.	1.25	0.5	0	....	....	....	1.75	Ref.	....	....	....	....	....	Ref.	1.75	0.15
77	..	..	12	3 mo.	2	0.25	0	....	....	....	2.25	0	0.25	0	....	....	....	0.25	2.5	0.21
78	+	..	12½	3 mo.	1	0.5	0.5	0	....	....	2	0.25	0	0	....	....	....	0.25	2.25	0.18
79	..	..	12½	2 mo.	1.25	0	Ref.	....	....	....	1.25	0.75	0.5	0	0.25	0	0	1.5	2.75	0.22
80	+	..	12½	4 mo.	1	0	0.5	0	....	....	1.5	0.5	0.25	0	....	....	....	0.75	2.25	0.175
81	+	..	13	3 mo.	0.5	1.5	0	0	....	....	2	0.5	0.25	0	....	....	....	0.75	2.75	0.21
82	..	..	13¾	5 mo.	0.5	0.25	0.25	0.5	0	....	1.5	0.25	0.25	0.25	0	....	....	0.75	2.25	0.165
83	..	..	14½	3 mo.	0.75	1.25	0	0	....	....	2	1.25	0	0	....	....	....	1.2 5	3.25	0.22
84	+	..	15	4 mo.	1	0.5	0	....	....	....	1.5	1	0	0	....	....	....	1	2.5	0.16
85	+	..	15	4 mo.	0.75	0.25	0	....	....	....	1	0.5	0.75	0	....	....	....	1.25	2.25	0.15
86	+	..	15	4 mo.	1.25	0.5	0	....	....	....	1.75	0.75	0.25	0.25	Ref.	....	....	1.25	3	0.2
87	..	..	15½	7¾ mo.	2.5	0.75	0	....	....	....	3.25	0	0	....	....	....	....	0	3.25	0.21
88	+	..	15¾	3 mo.	0.75	0.5	0.25	0.5	0.5	0	2.5	0.5	0.25	0	....	....	....	0.75	3.25	0.21
89	..	..	16	4½ mo.	0.5	0.5	0.5	....	....	....	1.5	0.25	1.25	0.5	....	....	....	2	3.5	0.21
90	..	..	16¼	3½ mo.	1.5	0.75	....	....	....	....	2.25	0.75	0	0	....	....	....	0.75	3	0.187
91	..	..	16½	6 mo.	0.75	0.5	0.25	0.25	0	....	1.75	0.5	0.25	0.25	0.5	0.5	0	2	3.75	0.23
92	..	..	16¾	4 mo.	2.25	0.5	0	....	....	....	2.75	0.5	0	0.5	0	....	....	1	3.75	0.2
93	+	..	17¼	6 mo.	1.25	0.5	0	0.5	0	0	2.25	0.25	0	0	0	....	....	0.25	2.5	0.145
94	..	..	17¼	7 mo.	1.5	1.75	0.25	0	....	....	3.5	0.5	0	0	....	....	....	0.5	4	0.23
95	..	..	17¼	5 mo.	1.25	0.75	0	....	....	....	2	0.5	0.25	0.25	....	....	....	1	3	0.177
96	..	..	17¼	5 mo.	1.5	0.75	1.25	0	....	....	3.5	Ref.	....	....	....	....	....	Ref.	3.5	0.2
97	..	+	17¼	11 mo.	1.25	1	0	0	....	....	2.25	Vom.	....	....	....	....	....	Vom.	2.25	0.13
98	..	+	17½	4 mo.	0.5	1.5	0.25	0	....	....	2.25	0.75	0	....	....	....	....	0.75	3	0.17
99	+	..	18¼	6 mo.	0.75	1.25	0	....	....	....	2	Ref.	....	....	....	....	....	Ref.	2	0.11
100	..	+	18¾	8 mo.	1.5	0.75	0	....	....	....	2.25	0.75	0	....	....	....	....	0.75	3	0.17

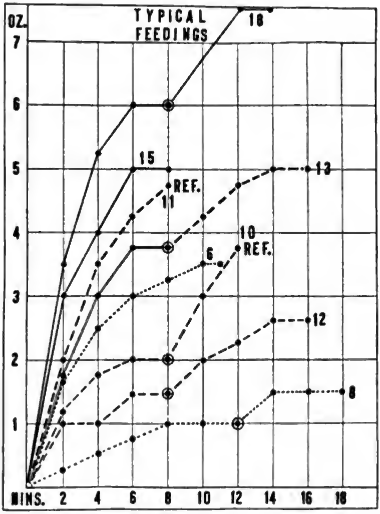

Fig. 4.—Some typical feedings. The numbers at end of each curve represent the weight of the baby. The point at which the second breast was begun is shown by the large circle. Various types of feedings are plotted. The curve marked 8 is a poor feeding, 1½ ounces from two breasts—and is very unusual because the milk was obtained at a steady rate from the first breast. The curve marked 12 is a fair feeding, 2¾ ounces from two breasts—rather irregularly obtained. The curve marked 10 is a good feeding, 3¾ ounces from two breasts. After twelve minutes the baby refused to nurse. The curve marked 6 is a good feeding, 3½ ounces from one breast, or 5.8 ounces per pound—this baby would have been as well off if he had been stopped at six minutes—with three ounces. Curve marked 13 is a good feeding from two breasts—3¾ ounces from first, 1¼ ounces from second, 3.85 ounces per pound. Curve marked 11 is a very good feeding from an abundant breast, 4¾ ounces in eight minutes. The baby refused to continue after eight minutes. This mother regularly supplied from four to five ounces in six minutes, on many observations. Curve marked 15 is a fair feeding but a baby who was doing very well. He probably obtained more at other nursings, since he obtained 5 ounces in six minutes. Curve 18—six ounces in six minutes, 1½ ounces from second breast. A very large thriving baby.

The poor feedings (Table 4, Fig. 3) again show the same general features. On the first breast the babies got from 80 to 90 per cent. of the milk in four minutes. The average emptying times were from four and five-tenths to five minutes.

The second breasts gave very poor feedings to all these babies, less than an ounce as a rule, most of which was obtained in two minutes. The average emptying time is very short (from two and four-tenths to four and two-tenths minutes). Only one baby obtained any milk after eight minutes and only three after six minutes. This group contains more older and larger babies when the milk would naturally be failing.

SUMMARY

From the above it is evident that nursing infants obtain the greater part of their feeding of breast milk in the first few minutes, from 40 to 60 per cent. in the first two minutes, and from 60 to 85 per cent. in the first four minutes. This holds true whether the supply is abundant, moderate or scanty. After eight minutes very few babies get any milk whatever. Only seventeen of our observations show any increase in weight after eight minutes; fourteen of these were from Tables 1 and 2—good feedings; only three babies obtained milk after ten minutes. A few larger, vigorous infants nursing from an abundant supply, may get small amounts of milk up to sixteen minutes.

The babies who need both breasts usually get less from the second than from the first side, except when one regularly yields a better supply. The rate at which a baby gets milk from the second breast is similar to that of the first breast: i.e., from 40 to 60 per cent. in the first two minutes and from 65 to 85 per cent. in the first four minutes. After that very little is obtained. The time after which a baby gets no more milk is usually shorter on the second breast than on the first.

The poor feedings have been completed in a shorter time than the good ones. When the breast supply is evidently failing, the baby gets all he can in from three to five minutes, as a rule. It does no good to leave a baby a longer time (from fifteen to twenty minutes) at a failing breast in the hope of eking out a meager supply.

If a baby empties the breast in from five to eight minutes and shows no signs of discomfort from an adequate feeding obtained in that time, there seems to be no good reason why he should not take his bottle in about the same time. If the nipple holes are of good size so that the milk flows freely, nearly all strong infants will finish the bottle in less than ten minutes. They evince less distress than the nurse does over the rapid feeding. On the other hand, a slow nipple either discourages the baby so that he will give up in disgust before he has finished the bottle, or else makes him swallow so much air that he vomits or has colic. We believe that from eight to ten minutes should be ample time for any but the feeblest infants to take a bottle.

CONCLUSIONS

The method of fractional weighing may well be applied to every breast fed baby since it is the only way by which we can determine how long a given baby should nurse, and whether he needs one or both breasts.

It seems fair to conclude that a normal baby who gets enough milk from one breast needs to nurse, as a rule, only from six to eight minutes, rarely from ten to twelve minutes.

A baby who needs both breasts may nurse from six to eight minutes on the first and from five to seven on the second. Very few babies need as long as ten minutes on a breast. A good many will empty the breast in four or five minutes.

There is no evident reason why a baby should not take a bottle feeding as fast as he does one from a breast.

INTRAVENTRICULAR AND SUBDURAL SERUM TREATMENT OF MENINGOCOCCUS MENINGITIS IN INFANCY *

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The treatment of meningococcus or epidemic cerebrospinal meningitis in infants, especially in the hospital class of patients, has not been entirely satisfactory. The mortality rate and the incidence of sequels, even with careful serum treatment, are too high. The results obtained at the Infants' Hospital in a series of cases treated by lumbar puncture before the use of serum did not differ materially from a series treated later with serum. In other words, for some reason, serum has not proved so helpful in the treatment of hospital infants as has been expected. Why this should be so has been a subject for consideration with us for several years that we might find a reason and hence improve the treatment.

It seems to us that two factors are responsible for a high rate of mortality and sequels in infancy. The patients are seen late or are admitted to the hospital after the meningeal symptoms are well pronounced. This means that it is already too late to give treatment for the stage of general infection of the disease by use of intravenous serum. It follows that the infant's resistance to infection is lowered by the delay, and also the local meningeal resistance. More important than the late admission or rather delayed treatment is the failure of the serum, as usually given, to reach the focus of inflammation, which is essential, for the antimeningococcic serum must come in contact with the meningococci. It is too late to give serum into the veins after the process is local in the meninges, as the serum is not filtered through the secreting apparatus in the brain in such a form as to be of any advantage locally.

The reasons for failure of the serum to reach the desired regions will be apparent, if some of the peculiarities of the meningeal involvement in infancy be considered. These peculiarities show why it is not easy for serum as given into the lumbar spine to reach all the inflamed areas. It appears that the principal lesions in infants are at the base of the brain, a so-called basillar meningitis. In consequence, depending somewhat on the amount of the inflammatory products, the arachnoid spaces of the spine are more or less shut off from those above. Hence,

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there is always some interference with the flow of the cerebrospinal fluid from above downward into the spinal spaces, at times amounting to a complete blocking. Another interference with the flow of the fluid may occur by closure of the foramina of Magendi and Luschka. These foramina are proportionally small in infants and are easily closed by adhesions or by products of inflammation. We have spoken of these peculiarities as interfering with the flow of the cerebrospinal fluid. It would seem natural to infer that whatever interfered with the flow of the fluid would also interfere with the dissemination of serum when introduced into the lumbar spine. Though the principal lesions are at the base of the brain, two other regions are involved which seem to us of great importance in infants and add much to the difficulty of the treatment. Inflammation of the ventricles appears early in the disease and naturally as the only approach to the ventricles is through the small foramina, there is little chance of serum given in the spine to come in contact with the organisms in the ventricles. The other region is the subdural space over the cortex. The fine adhesions found so commonly over the cortex of the brain of the normal infant favor the formation of pockets of inflammation, consequently serum introduced into the lumbar region cannot reach these cortical areas.

Another explanation has been offered for shutting off the foramina of Magendi and Luschka and also the spinal spaces from above. With increased tension in the ventricles the hemispheres are pressed against the skull and the exudate over the cortex is driven into the basal cisternae. This causes some interference with the absorption of the cerebrospinal fluid and with the circulation. These factors with the internal hydrocephalus, with the edema of the tissues, and especially with the distended posterior horns of the lateral ventricles cause the cerebellum to press against the medulla, hence shutting off the spinal spaces from above and partially closing the foramina. This is purely mechanical and may be entirely relieved as the case improves.

Taking these pathologic findings into consideration, it seems plausible that the difficulty in the treatment lies with the failure of the serum to reach the proper place. Even when fluid is obtained by lumbar puncture, we have reason to believe that serum introduced into the lumbar spine does not spread into the inflamed areas or go beyond the lowest level of inflammation and hence cannot do its work. Therefore, if the serum is to do its best work, it must be introduced above the block or partial block, flow over the inflamed areas, and, if possible, be drawn off by lumbar puncture.

Infants with open fontanels or cartilaginous fontanels offer easy approaches for giving serum from above. We began in 1914 to give serum for the treatment of meningitis into the lateral ventricles in cases in the wards at the Infants' Hospital. At first we hesitated to go into the ventricles unless we were unable to obtain fluid by lumbar puncture or unless the case did not improve with spinal serum. Later we found that resistant cases had infected ventricular fluid and we were ready to act more boldly though there might be good lumbar drainage. Now we consider it proper to give early intraventricular serum, especially if the fluid withdrawn is turbid indicating a ventriculitis, which commonly occurs in the first few days of the meningeal stage, if indeed, the ventricles may not be the first location attacked. We believe that early introduction of serum into the ventricles will prevent partial or complete blocking of the spine, which led us in the first place to consider intraventricular serum necessary. If there is complete blocking of the spines high and there is a dry lumbar tap, it is all the more necessary to give serum high above the block. There may be no interference with the passage of the fluid out of the ventricles through the foramina and serum introduced into the ventricles can flow out, clear up the meningitis, and later fluid be obtained by lumbar puncture. If the foramina are closed, it may be with inflammatory products only in conjunction with a ventriculitis or by a sagging as mentioned above and serum given into the ventricles can clear the ventriculitis and hence the passages.

The results of intraventricular injection of serum have been encouraging. The technic is easy and with ordinary care there is no danger. Directions are given in textbooks, and in articles on hydrocephalus, for puncture of the lateral ventricles, but it is necessary to vary according to circumstances. The needle should be of good size, at least 6 cm. long, and we prefer it without a stylet. The most important direction to remember is never to move the needle in a lateral direction after it is introduced through the skin. If it is desired to change the direction of the needle, pull it out and start again in the new direction. Only in this way can injury to the brain substance be avoided, for the fulcrum of its level is at the tough skin and any lateral motion of the butt of the needle will be as great or greater at the point. The needle should be introduced through the anterior fontanel at one side of the median line, far enough from the middle to miss the longitudinal sinus, and in a line joining the lateral angles. The direction should be a little forward and toward the outer canthus of the eye on the same side. It is never necessary to go in more than 4 cm., but if the ventricle is dilated, the distance is less in proportion to the dilatation. We think it better not to puncture both lateral ventricles at the same time, unless the opposite ventricle is not emptied or unless there is very thick fluid withdrawn from the first ventricle. The following case will serve to illustrate the necessity for ventricular serum:

CASE 1.—J. A., 6 months old, was admitted June 22, after an illness of ten days. Spinal fluid was purulent, under pressure, with many gram-negative intracellular and extracellular diplococci. Serum was injected intraspinally on successive days till June 25. Lumbar puncture, June 27: small amount of thick pus. July 2: dry lumbar tap. Fontanel bulging. Ventricular tap, fluid purulent, many organisms. With three intraventricular injections on alternate days the ventricular fluid cleared, and was free from organisms. Uneventful recovery. Last seen in June, 1921, and was in excellent condition.

There is an occasional case that persists in what might be called a chronic state. The patient is spastic, with slight fever or with normal temperature, is bright or lethargic. Organisms may be present in the spinal fluid but usually not; ventricular fluid negative; digestive symptoms of vomiting and poor appetite. Such cases resist serum given into the lumbar spine, and as the ventricular fluid is clear, they probably are resistant by reason of inflammation on the cortex not reached by the serum given.

In June, 1916, one of us (W. W. H.) injected serum in two such cases subdurally over the cortex at the outer angles of the fontanel. The first case showed a fall in temperature the day following the injection, and later a spinal fluid free from organisms. Unfortunately, the patient died a week later of bronchopneumonia. The postmortem showed the meningitis to have cleared.

The operation has been done many times since, and in some cases serum introduced subdurally has yielded marvelous results, and evidently reached a focus. The following case is mentioned to show the type of case and the results of treatment:

Case 2.—E. B., 7 months old, was admitted May 7. Onset said to have been two months previous. Patient was thin, emaciated, mentality slightly cloudy, neck stiff, extremities spastic, reflexes increased, fontanel bulging. Lumbar puncture: cloudy fluid; 7,000 cells; 66 per cent. polymorphonuclears; gram-negative intracellular diplococci. With spinal serum by May 15, the spinal fluid was negative. Bulging of the fontanel was relieved by lumbar puncture. The baby still was spastic, losing weight and vomiting. It was thought to be a feeble baby with a chronic fat indigestion, but there was no relief with changes in food. The vomiting, stiff neck, rigid extremities and increased reflexes persisted. June 21, subdural injection of 10 c.c. of the same serum was made into the spine. The serum was given on both sides at the same operation. Marked improvement resulted in two days. Vomiting ceased. The spasticity gradually cleared.

The technic of subdural injection is very simple. A 10 c.c. Luer syringe with a 16 gage needle is filled with serum. The puncture is made at the outer edge of the fontanel, so that the needle slips obliquely under the bone, thus making it easy to go through the dura. When through the skin and dura and in the subdural space, the plunger of the syringe will move in without force. The operation should not be attempted with a bulging fontanel, for with a brain pressing hard against the skull the serum will not distribute well, and there is some danger of increasing the local pressure, hence causing cortical lesions. Excessive fluid is withdrawn by lumbar or ventricular puncture before doing a subdural injection. If the ventricular fluid is cloudy and contains organisms, serum must be given into the ventricles as well as subdurally, for it is improbable that serum given subdurally will cure a ventriculitis.

During the years 1914-1920 there were treated in the wards of the Infants' Hospital eighty-one cases of epidemic cerebrospinal meningitis in infants under 2 years of age. Three of these infants were taken home against advice of the hospital, before sufficiently treated, and died within a few days. Seventy-eight received treatment as long as necessary in the hospital. Forty-two were treated by spinal serum injections alone, with a mortality of twenty-six cases, or 62 per cent. These were the ordinary favorable cases, and at the time no other treatment seemed necessary. The remaining thirty-six patients either did not improve with spinal serum, or, for other reasons found at examination, were not expected to improve, hence were given in addition to spinal serum injections, intraventricular or subdural injections, and sometimes both. There were nineteen deaths among the thirty-six, a mortality of 57.7 per cent. This indicates that we were able to get better results in the very ill than in the more favorable cases, by giving serum above the blocked or pocketed regions.

We were astonished, in following the cases to June, 1921, that many patients discharged "well" from the hospital developed hydrocephalus, deafness, blindness or some sad result. There appears to be, so far as we know, no way to determine if an infant is cured and in no danger of sequels, even if the spinal fluid becomes normal.

Thirty-three of the seventy-eight subjects were discharged from the hospital living and with negative spinal fluids, but eight of them died in from a few days to two years after discharge. Of these eight, three had spinal treatment only, five intraventricular as well as spinal treatment. One of the three spinal patients died of a relapse, one of empyema following measles, one a year and a half later of a complication following otitis media. Four of the five patients with intraventricular involvement died of bronchopneumonia several months after leaving the hospital and two of these showed normal brains at necropsy; the fifth returned to the hospital as a feeble feeding case with hydrocephalus, and obstructive hydrocephalus was found at the necropsy.

In June, 1921, we were able to account for the remaining twenty-five cases of the series. Fourteen patients are living and well; eleven are living but have serious sequels. The fourteen "well" cases are equally divided as to type of treatment, seven having received spinal injections and seven high injections of serum. This is a highly satisfactory result, for the ventricular and subdural cases were more discouraging at the start. However, the eleven cases with sequels tend to indicate the value of high injections in that six were spinal cases, supposed to be favorable at the start, and five were given high injections.

We have yet to see any harm done by careful intraventricular or subdural injection of serum, as shown clinically or by necropsy findings. Though the number of cases in this series may be rather small on which to base hard and fast conclusions, yet we are convinced from the study of these cases that the spinal introduction of serum is not sufficient, and in order to better the results, serum should be introduced into the ventricles early in the disease and repeated so long as the ventricular fluid is cloudy, or drainage from the lumbar spine is poor. The subdural injection of serum is indicated, when there is evidence of cortical irritation. Though it may seem radical, we believe that by the early high injection of serum, it would be possible in many cases to clean up areas of inflammation, which later cause mechanical and degenerative sequels.

THE INCIDENCE OF THYMIC ENLARGEMENT WITHOUT SYMPTOMS IN INFANTS AND CHILDREN *

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This report consists of an analysis of two thousand consecutive cases admitted to the University of Michigan Hospital during a period of nearly two years. The ages of these patients range from 3 days to 12 years. All infants and children coming to the hospital are first admitted to the pediatric clinic for examination, so that both surgical and medical cases are included in this group. Of the two thousand patients there were only three who came because of symptoms related to the thymus gland. A large number of patients with thymic symptoms were observed during this time, but are not considered in this report, as they were treated in the outpatient department and not admitted to the wards. The patients studied were those in whom there was no particular reason to suspect thymic enlargement from the history. The diagnosis rests on physical examination, roentgen-ray examination of the thorax, and in some instances postmortem examination.

A report of a special group of these patients, those with harelip and cleft palate, has already been published [1] in which the question of thymic enlargement in relation to operative procedures is briefly considered. Blackfan and Little,[2] in a study of sixty infants, found evidence of thymic enlargement in twenty-nine, or 48 per cent These infants were unselected cases and there was no reason to believe that the thymus gland was enlarged. In other words, they were so-called "normal infants" as far as thymic symptoms were concerned. They base their belief that the shadow found in roentgen-ray examination of these infants was due to an enlargement of the thymus on the following grounds: (1) The shadow disappeared after exposure to the roentgen ray. (2) It could not be distinguished from the shadow which at necropsy was proven to be cast by the thymus. (3) It is identical with that found in patients with clinical evidence of an enlargement of the thymus.

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[1] Greenthal and Lyons: Dental Cosmos **14**:186 (April) 1922.

[2] Blackfan and Little: Am. J. Dis. Child. **22**:495 (Nov.) 1921.

Blackfan and Little further state: "Whether this shadow should be interpreted as an enlarged thymus or whether it should be regarded as occurring normally in a certain percentage of normal infants cannot be stated at the present time." This report endeavors to show what happens to some of these "normal" patients with enlarged thymic glands during a period of unusual stress, such as surgical procedures and illnesses. It leads us to the belief that the finding of an enlarged thymic gland, even though there has been no clinical evidence of thymic symptoms, should not be regarded lightly. We have endeavored to check as far as possible the accuracy of the clinical and roentgenologic diagnosis of thymic hypertrophy, also to ascertain if the preoperative treatment of these patients is of any value in preventing "thymic" deaths, and to find out in what type of patient an enlarged thymus is most likely to be found.

In a discussion of the thymus, it is customary for most writers to state that at the present time the cause of so-called thymic death is not known. Some have even doubted whether the thymus per se is involved at all. However, the occurrence of an enlarged thymus, that is, a thymus gland which weighs more than the average, is frequently associated with the well known status thymolymphaticus and affords the best means of clinically recognizing this diathesis. It is also true that procedures which cause atrophy or fibrosis of this gland, such as radium and the roentgen ray, usually relieve thymic symptoms. We further believe that these same procedures may prevent the catastrophes which often affect persons with a thymolymphatic constitution. Argument for this belief will be discussed later.

In this series of two thousand cases a diagnosis of enlargement of the thymus was made clinically in ninety cases. This is an incidence of 4.5 per cent. The diagnosis was confirmed or made by means of the roentgen ray in each instance. A roentgenogram of the thorax was taken for various reasons in 351 patients of this series. The percentage of positive thymus cases among those in which roentgen-ray examination was made is, therefore, 25.6 per cent. The total incidence of enlargement of the thymus in these two thousand cases is, of course, too low. Had a roentgenogram been obtained for each patient, we would have found many more with enlarged thymic shadows. Yet Blackfan and Little found 48 per cent. of their sixty infants to have an enlargement of the thymus. We believe that the difference in our figures can be explained by the ages of the patients. In their series forty-five were under 4 months of age, and thirty-five were less than 2 weeks old. In our series the great majority of patients were more than 6 months old and some were as old as 12 years. Bovaird and Nicoll[3] have shown that the weight of the thymus is greatest at birth. Physiologically it diminishes about twenty per cent. during the first five years and further diminishes after this time.

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[3] Bovaird and Nicoll: Arch. Pediat. **23**:641, 1906.

In the accompanying table a list of the various conditions is given in which enlargement of the thymus was found. One is struck by the fact that many of the cases are associated with congenital defects and malformations. Of the ninety patients who showed enlargement of the thymus, forty-four, or 49 per cent., came to the hospital for the treatment of congenital malformations or defects. If we consider only the 351 patients of whom a roentgenogram of the thorax was taken, the total incidence of enlargement of the thymus is 25.6 per cent.

SHOWING THE VARIOUS CONDITIONS IN WHICH AN ENLARGED THYMUS WAS FOUND

Disease	No. of Cases	Disease	No. of Cases
Rickets	3	Congenital elevation of scapula	1
Harelip and cleft palate	24	Congenital hydrocephalus	1
Tuberculosis of spine	1	Sarcoma of the orbit	1
Congenital club feet	4	Hemangioma	3
Congenital malformation of extremities	3	Foreign body in esophagus	1
		Achondroplasia	1
Phimosis	2	Hereditary syphilis	2
Tonsils and adenoids	14	Empyema	1
Feeding regulation	2	Phlyctenular conjunctivitis	1
Thymic asthma	3	Foreign body in bronchi	2
Fracture of nose	1	Spastic paraplegia	1
Congenital goiter	1	Cretinism	1
Imbecility	2	Congenital dislocation of hips	3
Pneumonia	4	Hypospadias	1
Corneal ulcer	1	Lymphatic leukemia	1
Mastoiditis	1		

The frequency of enlarged thymus in infants and children with congenital defects is also shown by the following facts: In this series a roentgen-ray examination of the thorax was made in sixty-three patients with harelip and cleft palate. Twenty-four, or 38 per cent., showed thymic enlargement. In ten patients with spina bifida and club feet, seven, or 70 per cent., showed a shadow which was considered too broad. One hundred and ten patients coming for tonsil and adenoid operations had roentgenograms of the thorax. Of these only fourteen, or 13 per cent., showed enlargement of the thymus gland. It would seem, therefore, that congenital malformations and defects are frequently associated with thymic enlargement. This fact has been impressed on us so often that in the pediatric clinic we now have a roentgenogram of the thorax made of every infant and child with congenital malformations and defects and examined carefully for thymic enlargement.

A consideration that was of great interest to us in this analysis was the reliability of the physical examination and roentgen-ray diagnosis of thymic enlargement. In a patient who has never had thymic symptoms and who has not the appearance of a thymolymphatic status, the finding of an enlarged thymus may lead one to the belief that the shadow cast on the sensitized plate and the increased percussion dullness are due to other structures, such as the great vessels or glands. However, we found that the diagnosis was correct in the great majority of cases. The criteria of Blackfan and Little hold good in our series. We found that roentgen-ray treatment reduced the shadow. The shadow was exactly the same as that found in patients with clinical evidence of thymic enlargement. In this series seven patients showed no evidence of an enlarged thymus on physical or roentgen-ray examination. The necropsy confirmed this finding in each instance. In five patients thymic enlargement was discovered. The necropsy showed not only a hyperplastic thymus but the other findings of status thymolymphaticus. One patient in this series presented the physical findings of thymic enlargement and gave a characteristic history of thymic asthma. There was also a congenital heart lesion. This patient later developed bronchopneumonia and was admitted to the hospital. The roentgenogram of the thorax was entirely negative. Nevertheless, the patient received one treatment for the enlargement of the thymic gland as recognized by our examination. The necropsy, made one day later, showed a bronchopneumonia, congenital stenosis of the aortic isthmus, a hyperplastic thymus with some atrophy due to the treatment, and the other findings of status thymolymphaticus. For some unaccountable reason the roentgen ray failed to show either the enlarged thymus or the bronchopneumonia. Except for this one instance, necropsy has confirmed the roentgen diagnosis in every case in which it has been permitted.

The nutritional status of infants and children with thymic enlargement has also been a point of interest. It has been a popular conception that thymic enlargement occurred chiefly in well nourished persons. Our findings have for some time led us to believe that such is not the case, in which respect we again confirm the observations of Blackfan and Little. We have frequently found an enlarged thymus in poorly nourished and marantic patients and just as frequently have we found no thymic enlargement in well nourished infants and children. The nutritional status and bodily conformation have by no means given us the suggestion of lymphatism in a large percentage of the cases here recorded. It has suggested this state in a few instances.

We have necropsy reports on six patients observed during the time of this study, whose death may have been related to enlargement of the thymus gland or to status thymolymphaticus.

ABSTRACT OF CASES

CASE 1 (5381).—A boy, aged 12, was admitted to the hospital because of convulsions, defective vision, and a speech defect. The clinical diagnosis was epilepsy and motor aphasia with the possibility of a localized lesion in the brain. An exploratory decompression was performed but nothing abnormal was found. The patient died six hours after the operation. The necropsy report was: Status lymphaticus; lipoidosis of the suprarenals; persistent hyperplastic thymus. A roentgenogram of the thorax was not taken in this case.

CASE 2 (5376).—A poorly nourished baby, aged 6 weeks, was admitted to the hospital because of bronchopneumonia. Thymic asthma and a congenital heart lesion had previously been diagnosed. The roentgenogram of the thorax was negative for all conditions. The patient received one therapeutic roentgen-ray treatment the day before death. The necropsy report was: Thymicolymphatic constitution; hyperplastic thymus with roentgen-ray atrophy; acute bronchopneumonia; congenital stenosis of the isthmus of the aorta.

CASE 3 (5762).—A malnourished infant, aged 5 months, was admitted to the hospital because of hydrocephalus. The infant also showed signs of rickets. The report of the bacteriologic examination of the cerebrospinal fluid was a meningococcic infection. Following the second injection of serum into the ventricles, the temperature rose quickly to 107 F. and death occurred a few hours later. The findings at the necropsy were: Internal hydrocephalus; papilloma of the choroid plexus; status thymolymphaticus; hyperplasia of the suprarenals; rickets. A roentgenogram of the thorax was not taken.

CASE 4 (6241).—A boy, aged 3 years, was admitted to the hospital for removal of tonsils and adenoids. He also had achondroplasia. A roentgenogram of the thorax was taken in order to show the bony structures. No mention of the thymus gland was made in the report. The child died immediately after the operation. The necropsy report was: Marked thymic hyperplasia; thymicolymphatic constitution; hypoplasia of the suprarenals; achondroplasia. At our request the plate was re-examined several months later and a very definite shadow of an enlarged thymus gland was found

CASE 5 (6451).—A marantic infant was admitted to the hospital for severe diarrhea with toxic symptoms. After a stormy course during which time many infusions were given, the infant recovered and began to do very well at home. The baby was readmitted to the hospital at the age of seven months because of otitis media and pyuria. The patient was much improved four days later and had a normal temperature. Death occurred suddenly that day. The pathologist reported: Otitis media; lymphatic constitution; suprarenal hypoplasia with lipoidosis; hyperplasia of the thymus, especially of the medullary portion.

CASE 6.—A fairly well nourished infant, aged 3 months, was admitted to the hospital for the repair of a harelip and cleft palate. The roentgenogram of the thorax showed an enlarged thymus. The patient received two pre-operative treatments at weekly intervals and then was operated on successfully. The convalescence was rapid and uneventful. Two months later the patient was scheduled for the second operation. He was found dead in bed the night before he was to be operated on. At necropsy the following diagnosis was made: Thymicolymphatic constitution; hyperplastic thymus (cortex only); lymphoid hyperplasia; suprarenal hypoplasia; cardiac dilatation; pulmonary congestion.

Does the preoperative roentgen-ray treatment of patients who have enlargement of the thymus gland lower the number of operative deaths?

We believe that it does, although it is very difficult to prove this point definitely. In this series of cases there was no immediate death following operative procedures in patients treated before operation. There also were no sudden deaths in the patients who did not show enlargement of the thymus. It seems more than a coincidence that the patients who died suddenly after operative procedures all showed a thymolymphatic constitution and none of them had been treated. Yet these facts do not justify a dogmatic statement that the mortality rate has been lowered because we have treated the patients before operation. We do not know what would have happened had these patients received no treatment. Statistics, too, are unreliable. It has been our impression, and that of others in the hospital, that the immediate mortality rate following operation in infants and children has been lowered, but there are so many other factors which may play a part, such as better technic and anesthesia, better preoperative care, different types of cases, etc., that we cannot be sure.

It is quite certain that all patients with enlargement of the thymus do not die when operated on. A little boy whose general appearance and physical examination suggested thymic hyperplasia came into the hospital for circumcision. A roentgenogram of the thorax was ordered to confirm our diagnosis. Through a misunderstanding the patient was operated on before the picture was taken. The operation and his convalescence were uneventful. The roentgenogram was then taken and disclosed an enlarged thymus for which he was treated. A little girl, aged 2 years, with a long standing pyuria was admitted for cystoscopy. There was nothing in her history to suggest thymic enlargement. While under the anesthetic she had a convulsive seizure. A roentgenogram of the thorax disclosed an enormous thymic shadow for which she was treated. Gerstley [4] reported an interesting case, that of a little boy who was known to have thymic enlargement. He needed a tonsil operation very badly. This was done and no untoward results occurred.

On the other hand, it seems reasonable to give these patients the benefit of a treatment which we know will reduce the size of the thymus gland. We are aware of the marked reduction in size of the thymus that can be secured when patients with thymic symptoms are exposed to therapeutic roentgen rays or to radium emanations. We know of no reports of harmful effects following this form of treatment of the thymus and we have never observed any in this clinic. Because some patients with thymic hyperplasia go through operations or severe illnesses without trouble, does not mean that all will do so. We have no means of knowing beforehand who will be the fortunate ones. It would seem, therefore, that the reduction of an enlarged thymus is indicated in all patients before operation.

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[4] Gerstley: M. Clinics N. America **5**:245 (July) 1921.

How shall we treat nonoperative cases which show thymic enlargement? We have given all these patients roentgen-ray treatments in order to reduce the size of the gland. It is our belief that this, too, is a beneficial procedure. It has long been known that some patients with enlargement of the thymus react to illnesses in a violent manner. For example, an infant aged 9 months contracted pneumonia. The temperature quickly rose to 106 F. and death occurred in two days. The necropsy showed a large hyperplastic thymus, status thymolymphaticus, an extensive pneumonia with beginning empyema on the right side. A malnourished infant contracted pertussis and later lobular pneumonia. At the end of the second week the temperature rose to 106 F. and the infant had a series of convulsions with temporary cessation of respiration each time. The infant finally recovered, except for a marked stridor and rapid respirations. A roentgenogram taken at this time showed thymic enlargement. After the gland had been reduced in size the stridor disappeared and the respirations became normal.

What happens to these patients with thymic enlargement and no symptoms if they are left untreated? In many instances the gland undergoes a gradual physiologic atrophy and nothing happens. In other cases, the thymus enlargement persists into adult life and may then cause symptoms. "Thymic" deaths have been observed in adult patients at this hospital since we have been paying particular attention to this subject. During the influenza epidemic of 1918, we cared for soldiers in our wards. Many of the fatal cases showed a persistent hyperplastic thymus at autopsy.

It would seem advisable to watch persons in whom thymic hypertrophy is detected. If they develop symptoms they should be treated at once. If one does not think it advisable to reduce the size of the gland, frequent examinations should be made to determine whether the thymus is undergoing the normal gradual atrophy. If it is not, it should be treated.

CONCLUSIONS

1. In a series of two thousand consecutive hospital admissions, thymic enlargement was diagnosed in ninety, or 4.5 per cent. Of these ninety patients, eighty-seven gave no history or presented no symptoms of thymic involvement.

2. Enlargement of the thymus was noted in 25.6 per cent. of all the patients who had a roentgenogram of the thorax made.

3. Patients with congenital defects and malformations are more apt to have thymic enlargement than are other patients.

4. It is possible that the mortality rate of operated cases was lowered by preoperative thymic treatment.

5. It would seem advisable to give thymic treatment to persons with thymic enlargement, even though they have no clinical evidence of thymic hyperplasia.

CLASSIFICATION AND MANAGEMENT OF ASTHMA IN CHILDHOOD*

THE IMPORTANCE OF RABBIT HAIR AS A CAUSE IN NEW YORK CITY

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It was deemed worth while to publish a report of the first one hundred cases seen in the Children's Asthma Class at Bellevue Hospital on account of the unusually high percentage of positive reactions to animal emanations. The report also emphasizes the necessity of separating true asthma from chronic pulmonary infections in children.

The consideration of asthma and allied conditions has been reviewed so often and so thoroughly of late that no attempt will be made to summarize the literature on the subject.

Diagnosis.—The classification of the cases into either sensitive or nonsensitive was not usually made until the patients had been under observation for some time. The patients were given the telephone number of one of the attending physicians and urged to call him at the onset of an attack. Whenever possible, a visit was made at once and, though this was not practical in every case, an effort was made to study the type of the attack and only thereafter was a definite diagnosis made.

The cases seen were placed in one of two groups according to the following clinical findings:

SENSITIVE TYPE	NONSENSITIVE TYPE
1. COURSE OF THE DISEASE	
Periodic attacks with complete or nearly complete cessation of pathologic signs between the attacks.	Either chronic cough without dyspnea or periodic remissions with moderate dyspnea but the pathologic signs tended to remain constant between the remissions.
2. TYPE OF THE ATTACK	
Onset in which dyspnea was the most prominent symptom. This was usually characterized by slow, labored breathing with prolongation of the expiratory phase up to the beginning of the inspiratory phase so that there was no period of rest between. Cough was not prominent at first but later, after the dyspnea had begun to subside, it became more prominent and	In those with periodic remission cough at the onset was the most prominent symptom. Dyspnea, if it appeared came on from twenty-four to forty-eight hours later and was not as severe as in the sensitive type. It also had a tendency to be more inspiratory in type. On auscultation during the attack the râles were often very similar to those found in the sensitive

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* From the Children's Medical Division of Bellevue Hospital.

SENSITIVE TYPE	NONSENSITIVE TYPE
2. TYPE OF THE ATTACK—(*Continued*)	
lasted after the dyspnea had entirely disappeared. On auscultation in the early stages the râles were similar in all parts of the chest and occurred about equally during all parts of both inspiration and expiration. Toward the end they became looser and were patchy in their distribution, resembling those of simple bronchitis. There was usually acceleration of the pulse rate but no rise in temperature.	type and later also showed a loose quality, but between the attacks these showed a tendency to remain constant though fewer in number. There was nearly always acceleration of the pulse rate accompanied by a rise in temperature.
3. DURATION OF THE ATTACK	
This varied from a few minutes to a few days and was followed by a relatively rapid convalescence.	This varied from a few days to a week or more and convalescence was relatively slower.
4. QUALITY OF THE SPUTUM	
When obtained this showed a fairly clear gelatinous material with small opaque bodies, Laennec's pearls.	This was slightly more profuse, was thick, yellow or greenish, and purulent.
5. BEHAVIOR TO EPINEPHRIN	
Intramuscular injections of a solution of epinephrin chlorid, 1:1,000 gave marked immediate temporary relief.	The relief obtained was not as marked.

The two types are often extremely hard to differentiate as, after repeated frequent attacks, the sensitive type may have many signs of a subsequent bronchitis which, however, finally clears up when the attacks cease. Roentgen-ray examinations were made of every case as a routine as well as total and differential white blood cell counts. The differential cell count in the sputum showed a high percentage of eosinophils in both types. These criteria were found of only occasional value in making the diagnosis. It is perhaps well not to draw a hard and fast line between the two. It is only by taking all factors into consideration that the impression is gathered that the child adheres more to one group than the other. No one factor is sufficient to make the diagnosis and all factors are not found in every case.

It is interesting to note that in the sensitive group the average age of onset was 3.7 years, the earliest case occurring at birth and the oldest child being 9 years of age. The average duration was 5.92 years. In the nonsensitive group the average age of onset was 3.42 years, the youngest patient being aged 3 months and the oldest 11 years. The average duration was 4.02 years.

Skin reactions to proteins were performed at the clinic and using these in conjunction with the clinical findings the cases were classified as follows:

Group I, sensitivity determined, 44 cases; group II, sensitive type but reactions negative, 12; group III, chronic bronchitis, 33; group IV, not sufficiently tested to classify, 11. Total 100 cases.

GROUP I.—*Sensitivity determined.*—Of the forty-four cases in which sensitivity was determined, thirty-one, or 70 per cent., gave positive skin reactions to one protein, and thirteen, or 30 per cent., gave reactions to more than one protein. The number of reactions tried on each patient varied from seven to forty-five. When there was a definite history of contact with a certain protein followed by symptoms and when a definite skin reaction to that protein was obtained, it was not considered necessary to try further tests.

In this group the reacting proteins were:

Rabbit hair, 32 positive reactions; horse dander, 8; cat hair, 6; dog hair, 1; guinea-pig, 1; feathers, 1; foods, 8; pollens, 3; total, 60 positive reactions.

Of sixty positive reactions obtained, thirty-two, or 53 per cent., were from cases which showed sensitivity to rabbit hair. Walker,[1] on the other hand, said, "Of the animals, the horse is the chief cause and the cat is a frequent cause; other animals play a minor rôle." The possible significance of this will be discussed later.

The skin reactions were performed by the standard scratch method and read at the end of twenty minutes. No one of the reactions included was less than two plus and the majority were four plus.[2] Wherever possible, every positive reaction was checked by an intracutaneous test, using solutions supplied by Dr. Coca. The two methods cannot be compared directly as shown in a previous paper.[3] In the present series the sensitivity as determined by the two methods agreed in twenty-nine persons. In several instances one sample of a dry commercial preparation would give a negative reaction, whereas another sample from the same commercial house would give a definitely positive reaction. These preparations were tested repeatedly on sensitive subjects. Some of the powders which failed to react were from fresh lots. It was, therefore, not a question of age or dampness. In one instance, three different samples failed to react, whereas a fourth preparation gave a definite reaction. There was no apparent difference in these preparations in gross appearance or solubility and the positive reaction was obtained with a powder bought four months before two of the others which gave no reactions.

Pseudoreactions were not uncommon with both methods. These reactions were moderate in size, definitely larger than the controls and sometimes showed pseudopods. Repeated skin tests on different days proved them to be negative. This type of reaction may well account for some of the results obtained on normal children by Baker[4] and by Peshkin and Rost.[5]

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[1] Walker, I. C.: The Cause and Treatment of Bronchial Asthma, M. Clin. N. America **1**:1177 (Jan.) 1918.

[2] In the cutaneous method one plus was used to indicate a reaction in which the wheal measured from 0.5 to 1.0 cm.; two plus, from 1.0 to 1.5 cm.; three plus from 1.5 to 2.0 cm., and four plus, above 2.0 cm.

[3] Larsen, N. P., Alexander, H., and Paddock, R.: Bronchial Asthma and Allied Conditions, J. Immunol. **7**:81 (March) 1922.

Several cases showed positive skin reactions to proteins which had no relation to the production of symptoms. This has also been reported by Walker, Caulfeild and others. On the other hand, in two cases of food sensitivity, attacks regularly followed the ingestion of certain foods, but all skin tests remained negative.

These variations emphasize the fact that the skin reaction is merely one factor in making the diagnosis. Whether positive or negative, the skin test must not be allowed to outweigh all other contradictory evidence.

In all these cases an attempt was made to trace possible contact with the reacting protein, either in the home or in the environment. In thirty-two cases, or 73 per cent., the source of the protein was found. In rabbit hair cases the source was found in pillows, mattresses, comforters, collars on coats, hats, muffs, playthings, chest protectors, rabbits as pets, and unskinned rabbits brought into the home for food. In some homes the amount of rabbit hair was really astonishing. One father brought to the clinic nine samples from different pillows and mattresses in his home, all of which contained either pure rabbit hair or a mixture of rabbit hair with feathers or cotton. With one girl the attacks of asthma were definitely identified with the wearing of a hat which had been bought as a "beaver" hat. When bits of hair from this hat were teased out and put under the microscope they were found to be of two different types; the long silky hairs on the surface were from some animal other than a rabbit and very closely resembled cat hairs, but deeper, in the more densely matted or felt part of the hat, the material was undoubtedly rabbit hair. Eight cases of this type of asthma have been described by Ratner,[6] one of which was also caused by a felt hat.

The method of identifying epidermals is worthy of note. The microscope is invaluable and it is well to have on hand samples of known epidermals for comparison. A small amount of the unknown material is placed on a slide and a drop of 70 per cent. alcohol allowed to fall on it. This flattens the material and when the alcohol has almost evaporated another drop of a weak solution of alakali is added and a cover slip placed on this. More permanent slides must be imbedded in glycerin or balsam. On such a slide rabbit hair has a characteristic appearance. In the finer or down hairs the cells are in single layers and when the sides of these are examined the margins of the cells are seen to overlap, giving an imbricated or shingle-like appearance. These form tiny barbs along the hairs and though this is true to a certain extent of all hairs, the barbs are rather more prominent in rabbit hair. It is the interlocking of these barbs that gives the strength and firmness to commercial felt.

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[4] Baker, H. M.: Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **19**:114 (Feb.) 1920.

[5] Peshkin, M. M., and Rost, W. L.: The Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **23**:51 (Jan.) 1922.

[6] Ratner, B.: Rabbit Hair Asthma in Children, M. Clinics N. America **5**:1129 (Jan.) 1922.

Treatment.—The most rational method of treatment, as shown by Cooke and others, is to remove the offending protein from the environment of the sufferer. The result is usually very striking. Complete desensitization as produced by Schloss[7] in a food case is apparently not readily obtained in persons sensitive to inhaled proteins. This has been repeatedly shown in pollen cases. These must be reinjected each year. Walker[8] published a series of twelve animal hair cases treated with gradually increasing doses of the offending protein with very good results. He concludes, "Patients whose asthma is due to the protein of horse dander and cat hair are relieved of asthma by subcutaneous injections of these proteins. The more thorough the treatment the more permanent the relief." Longcope[9] reports a case of chicken feather sensitivity in which asthma had existed for nineteen and a half years. After twenty-one injections, the highest being 0.5 c.c. of a 1 : 500 solution of the protein, the patient remained well. The removal of the feathers was not mentioned.

In the present series an attempt was made to remove the offending protein from the home in every case. Injections of a solution of rabbit hair protein, however, were also given to twenty children who were sensitive to this protein. This was done for several reasons. First, it at least produces an increased tolerance toward the offending protein, if not complete desensitization. Secondly, the repeated injections give an opportunity to teach the patient how to control his asthma. Just as a tubercular patient is taught how to care for himself, so an asthmatic must be taught to watch carefully for possible harmful protein contact. This is only accomplished after repeated visits. Thirdly, it helps to keep the case under continued observation. Lastly, the psychic effect that something definite is being done undoubtedly gives the subjects a happier point of view and a better chance to live a more normal life.

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7. Schloss, O. M.: A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**:341 (June) 1912.

8. Walker, I. C.: Treatment of Patients with Bronchial Asthma with Subcutaneous Injections of the Proteins to which they are Sensitive, J. M. Research **36**:423 (July) 1917.

9. Longcope, W. T.: Protein Hypersensitiveness and its Importance in the Etiology of Disease, J. A. M. A. **77**:1535 (Nov. 12) 1921.

Just what rôle the injections had in the results obtained is hard to determine. Most of the patients were started with 3 minims of a 1 : 100,000 solution and carried through several injections of a 1 : 500 solution. The injections were increased from 1 to 3 minims per week. Of the twenty children who received injections, one child failed to show any improvement and three showed only slight improvement. In two cases in which no rabbit hair was found in the home, attacks ceased after the first injection. To date, a period of nine months, there have been no further attacks. Prior to this attacks had been almost constant, in one of the cases for three years, in the other for four years. In twelve cases in which the protein was located and removed immediate relief followed. These patients, however, were also given injections. Two other patients who came irregularly to the clinic showed about 50 per cent. improvement.

All the injected subjects were tested repeatedly to note the effect on the skin reaction. Individual skins, or perhaps individual sites on the skin, showed considerable variation in the size of of the reaction at various times. There was, however, no constant decline. At the end of the series in no case was there a change in the size of the skin reaction as far as the diagnostic test was concerned. No attempt was made to see if the reaction had changed as regards dilute solutions. Walker [10] showed a great decrease in the reaction to the dilute solutions in his pollen series and [8] a disappearance in some of his dander cases, after a series of injections.

One of the patients who was sensitive to timothy had been well for three seasons in a timothy district and for eight years previous to this time had suffered from typical early hay-fever. Nevertheless, he gave a markedly positive skin reaction to timothy. The relation between the size of the skin reaction and symptoms is still open to question.

Group II.—In this group were placed twelve cases in which all evidence pointed to a definite protein sensitivity. All skin tests were repeatedly negative.

Group III.—*Chronic Bronchitis.*—Of the thirty-three cases in this group none showed positive skin reactions.

Treatment.—For the first year at the clinic it was decided to find out what this group would do under general care. This consisted in:

1. Removal or treatment of any points of focal infection that could be found along the respiratory tract.

2. Home hygiene or country visits for as long as possible.

3. Rest.

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[10] Walker, I. C.: Frequent Causes and the Treatment of Seasonal Hay-Fever, Arch. Int. Med. **28**:71 (July) 1921.

4. Open air classes in school, the diet being also increased by additional food.

5. Cod liver oil preparations.

At the end of this year it is felt that eighteen of the thirty-three patients show enough improvement to warrant their being classed as distinctly improved, as against fifteen whose condition has remained unchanged. Of those improved, ten have shown an absolute cessation of all attacks and pathologic signs, while eight seem to be improved but still show some attacks and pathologic physical signs.

As the quality of improvement is an extremely difficult factor on which to base conclusions, great care has been used in making this summary and the feeling is held that if any error has been made it is on the side of conservatism. A substantial proportion of this group would seem to yield to simple hygienic measures without specific treatment. It would be well to keep this proportion in mind in drawing conclusions from cases treated with vaccines.

Group IV.—In this group were placed cases which might belond to either Groups I, II or III, but due to insufficient observation it was not possible to classify them. Eleven cases were placed in this group.

DISCUSSION

A comparison of this series with some of the others already published is shown in the accompanying table.

Comparison of Cases Reported by Various Observers

Author	Number in Series	Number Giving Positive Reaction to Protein	Per Cent. of the Number in Series	Number Positive to Animal Emanations	Per Cent. of the Number Giving Positive Reaction to Protein	Number Positive to Rabbit Hair	Per Cent. of the Number Positive to Animal Emanations
Cooke [11]	327	240	73.4	138	57.5	18	13.0
Rackemann [12]	150	74	49.3	37	50.0	..	....
Rackemann [13]	301	194	64.1	55	28.3	..	....
Scheppegrel [14]	1,000	...	....	7	0.7	..	....
Walker [8]	...	40	....	12	30.0	..	....
Walker [15]	400	191	47.75	78	40.8	..	....
Walker [15] (cases below 15)	136	94	69.1	51	54.3	..	....
Present series	100	44	44.0	36	81.8	32	88.8

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[11] Cooke, R. A.: Studies in Specific Hypersensitiveness, J. Immunol. **7**: 147 (March) 1922.

[12] Rackemann, F. M.: A Clinical Study of One Hundred and Fifty Cases of Bronchial Asthma, Arch. Int. Med. **22**: 517 (Oct.) 1918.

[13] Rackemann, F. M.: A Clinical Classification of Asthma based upon a Review of Six Hundred and Forty-Eight Cases, Am. J. M. Sc. **162**: 802 (Dec.) 1921.

[14] Scheppegrel, W.: Asthma and Hay-Fever, Philadelphia, Lea & Febeiger, 1921.

[15] Walker, I. C.: A Clinical Study of Four Hundred Patients with Bronchial Asthma, Boston M. & S. J. **179**: 288 (Aug. 29) 1918.

These different series include subjects exposed to different environments. Those in the present series, living in crowded quarters on the lower East Side of New York City, were, as has been shown, exposed to large quantities of rabbit hair. The cases (from New Orleans) in Scheppegrel's series [14] were undoubtedly exposed to greater concentrations of pollens. The environments of the others are not known but were, no doubt, different from the lower East Side of New York City.

Cooke and Vander Veer,[16] in reviewing their series of cases, remarked, "The mere fact that over 42 per cent. of a large number of sensitization cases are clinically multiple in type suggests very strongly the fact that such individuals as a group, possess a very peculiar capacity to become sensitive in a natural way, to certain proteins to which their environment and habits of life frequently expose them, and reasoning from analogy then we might expect that any form of foreign protein parenterally introduced would readily render them acutely sensitive." In one series of nonsensitive subjects and another series of sensitive subjects they compared the effect of the introduction of foreign serum. The two groups, however, showed practically no difference. They conclude that, "evidently the type of clinical sensitization that they (patients) acquire and maintain is dependent upon some other factor than the mere parenteral injection of native heterologous protein."

Although the present series is too small to warrant any definite conclusions yet added to the evidence that a very high percentage of patients react to a number of proteins, it certainly suggests the possibility that the type of protein in the environment may have some relation to the subsequent sensitivity. One can hardly exclude this evidence because of the fact that one series of cases which received one or two small subcutaneous injections of serum failed to show increased symptoms following their injections. Perhaps, it is necessary that the protein be in the environment during a long period of time or at a certain time in the individual's life, as for instance, during the course of whooping cough or other severe respiratory infections. It is well known that a certain number of patients date the onset from a period immediately following an acute respiratory infection.[1] Referring to ingested proteins, Talbot [17] says, "Injury to the mucous membrane is probably necessary, except shortly after birth, before the foreign protein can be absorbed unchanged. The greater the injury to the intestinal mucous membrane the more easily can foreign protein pass through the intestinal wall. The younger the infant is the more easily can a foreign protein pass through the healthy, uninjured, mucous membrane." This may be also true of the mucous membrane

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16. Cooke, R. A., and Vander Veer, A. Jr.: Human Sensitization, J. Immunol. **1**:201 (June) 1916.

17. Talbot, F. B.: Asthma in Children. Its Relation to "Egg Poisoning" (Anaphylaxis), Boston M. & S. J. **171**:708 (Nov.) 1914.

of the respiratory tract. An observation which seems to contradict this, however, is the following: A medical student known to be definitely sensitive to lobster and ragweed worked for a drug concern. One of his duties consisted in grinding urease into a very fine powder. He did this for a few days at a time every two or three weeks. He worked from April until July without symptoms. In July, as he poured the fine powder into a container, he had symptoms for the first time. These consisted in sneezing, coughing and burning of the eyes. A skin test was tried and gave a positive reaction to urease. From then on, each time he was exposed to the powder he suffered from the same symptoms. Unfortunately, no skin test had been tried with this substance prior to the onset of symptoms.

More evidence is necessary before definite conclusions should be attempted. At present, however, it seems probable that the concentration of a protein in the environment of a child with a tendency to develop sensitivity has something to do in determining what specific protein or proteins will later affect him. This would explain multiple sensitivity as well as the great variety of results in the different published series.

SUMMARY

Of one hundred cases of asthma and chronic bronchitis referred to the class, forty-four subjects were shown to be sensitive to protein. Of the forty-four, thirty-six were positive to animal emanations and of these thirty-two were positive to rabbit hair.

Sixty positive reactions were obtained. Of these forty-nine, or 81 per cent., were positive to animal emanations and thirty-two, or 54 per cent., were positive to rabbit hair.

In treating the sensitive type, removal of the protein from the environment gave marked immediate relief.

In treating the nonsensitive type, simple hygienic measures gave relief in slightly more than half the cases.

BOOK REVIEW

INDIVIDUAL GYMNASTICS. By LILLIAN CURTIS DREW.

This book should easily prove to be a useful and practical text, and should be welcomed and appreciated by both physician and educator. It fills a real need admirably, and intelligibly covers a field which is quite foreign to all but a few persons. The particular value of the book lies in the fact that it deals exhaustively with the unusual type of case and details methods and forms of treatment suitable to the individual case. This is the type of help really wanted, but only too commonly missed in the average text. All directions are concise and clear, therefore easily understood and applied. The chapters on posture are particularly good. This is fortunate in view of the fact that the subject has received considerable attention in recent pediatric literature, and is considered important. Another excellent chapter is the one on shoes and correct exercises for the feet. The style throughout the book is simple and direct. The illustrations are mostly in the form of diagrams and are fairly adequate. There are comparatively few actual photographs. The absence of these is noticeable in view of the fact that the subject matter lends itself particularly well to this form of illustration. It is probably the only shortcoming of this excellent little book.

CORRECTION

In the paper by Dr. Ludo von Meysenbug entitled "The Inorganic Phosphate Content of Breast Milk of Mothers With Normal and With Rachitic Infants" appearing in the *American Journal of Diseases of Children*, September, 1922, page 200, the last sentence of the paragraph before the summary on page 202 should read "14.8 mg. phosphorus per hundred cubic centimeters" instead of "7.4 mg."

American Journal of Diseases of Children

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THE VITAL CAPACITY OF THE LUNGS OF CHILDREN IN HEALTH AND DISEASE *

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MINNEAPOLIS

As a result of recent investigations, the clinical value of the determination of vital capacity in diseases of the heart and lungs has attracted attention, especially since this measurement is often found to be greatly reduced by various pathologic conditions of these organs. It has long been recognized, however, that in order for the determination of the vital capacity to be of any great practical value, it is necessary, first, to determine the normal relationship existing between it and other body measurements. Investigators, therefore, have attempted to establish normal standards for vital capacity based on age, height, body weight, stem length, trunk volume and surface area, but in most instances have neglected to determine the extent of normal variability. Since for any body measurement the lung capacity is known to show a certain amount of variability, it is clear that in order to detect abnormal fluctuations, the extent of normal variability must be determined first. Therefore, in connection with the study of vital capacity for children, an attempt is made to estimate the extent of normal variability during childhood. I am indebted to Drs. R. E. Scammon and Wm. Hart for valuable advice concerning the statistical treatment of the data presented in this paper.

1. *Material and Methods.*—Observations are reported for 2,509 normal and healthy children, 1,289 boys and 1,220 girls, ranging in age between 4 and 19 years inclusive. The data (sexes separated) are averaged according to age in Tables 1 and 2, according to standing height in Tables 3, 4, 5 and 6, according to sitting height in Tables 7, 8, 9 and 10, and finally according to body weight in Tables 11 and 12. In addition, observations are recorded for fourteen boys and twenty-six girls (Table 13) afflicted with mitral insufficiency of varying degrees of severity; for seventeen boys and fourteen girls (Table 14) suffering from acute bronchitis; for four boys and five girls (Table 15) with pneumonia; for thirteen boys and four girls (Table 16) subject to asthma; and lastly for seventy-nine boys and seventy-one girls (Tables

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17 and 18) having tuberculosis. The total of all the observations for vital capacity, including both the normal and also the pathologic cases, amounts to 1,420 with the boys and 1,342 with the girls, a grand total of 2,762 cases.

The vital capacity was measured by means of an accurately calibrated wet spirometer, which offered very little resistance to expiration. The children were carefully instructed to take the deepest possible inspiration, and to empty the lungs completely into the spirometer. As a rule, small groups were taken at a time, so each subject understood from observation how to cooperate to the best advantage. Every child was permitted several trials, and the maximum repeatedly expired was recorded as the vital capacity. The children were urged to do their best, and usually the spirit of competition was sufficiently keen to make one reasonably certain that the records obtained represent the best effort they were capable of exerting. In instances where the cooperation of the child was unsatisfactory, the data were discarded. Furthermore, children having an unusually low vital capacity were included in the averages only in case they gave no history of chronic heart or lung disease. So far as possible all children suffering from acute respiratory infections were excluded from the averages. The vital capacities recorded are not corrected for temperature, aqueous vapor tension, or for variations in barometric pressure.

The children were weighed wearing their ordinary indoor winter clothing. In order to obtain the net weight, the weight of the clothing (computed as recommended by Bardeen[1]) is deducted from the observed gross weight. The standing height (in stocking feet), and also the sitting height (measured with the children seated against a perpendicular scale) was recorded for each child in the majority of instances.

In the analysis of the data for the normal children, as averaged according to age, standing height, and stem length, in each case statistical methods are employed to calculate the degree each average might be expected to fluctuate were observations obtainable upon an infinitely large number of comparable series of cases, and also to determine the extent of absolute and relative variability of vital capacity, by the estimating of the probable error, the standard deviation, and by computing the coefficients of variation, respectively.

The possibility of deriving the approximate normal vital capacity by the estimating of the probable error, the standard deviation, and for any known age, standing height, sitting height, or weight, by means of empirical formula is discussed later on.

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[1] Bardeen, C. R.: Weight for Height charts for school boys and girls, Bull. Univ. Wis. Beyer: Growth of U. S. Naval Cadets, Proc. U. S. Naval Inst. **21,** 1895.

2. *Vital Capacity and Age.*—The averages for the vital capacity of the lungs at different ages, as estimated from the nearest birth day, are recorded in Tables 1 and 2. Since there is a sexual difference in vital capacity at corresponding ages, the data for the boys and girls are averaged separately in the tables. In most instances the number of subjects in each group is sufficiently large to render the means fairly significant, especially for the boys from 6 to 16 years, inclusive, and for the girls from 6 to 15 years. For the other groups the averages recorded are probably of less significance, due to the fact that they include relatively fewer observations.

Between 6 and 16 years of age, inclusive, the average vital capacity of the lungs with the boys (Table 1) shows an increase from 1,154 to 3,425 c.c., the absolute gain during the ten years amounting to 2,271 c.c. When expressed in terms of relative increase, this gain amounts to about 197 per cent. Consequently, at 16 years of age the average vital capacity for the boys is practically three times as great as the initial value at 6 years.

With the girls between 6 and 16 years of age, inclusive (Table 2), the average vital capacity increases from 1,085 to 2,778 c.c. The absolute gain in this case amounts to 1,693 c.c., or approximately 578 c.c. less than the increase registered by the boys during a similar period. The relative increase for the ten years amounts to approximately 156 per cent. with the girls, as compared with 197 per cent. gain for the boys. Consequently, at 16 years of age the vital capacity with the girls is only two and one-half times as great as the initial 6 year average.

As is true of physical measurements in general, the vital capacity likewise fluctuates within rather wide limits. Thus, at practically each age the maximum vital capacity recorded (Tables 1 and 2) is two or more times as large as the minimum observed. On inspecting the individual data, however, it is found that in many cases these extreme variations in lung capacity at each age, paralleled to some extent the individual's variation in size from the average of his respective groups. Thus, the unusually low vital capacities recorded, were obtained, as a rule, from children considerably below the average size for their age, whereas the maximum readings were usually for children considerably larger than their group average. The absolute extent of the variation becomes larger as the vital capacity increases, and also is usually greater for the boys than for the girls of corresponding age. Although absolute variability evidently increases with age, and differs for each sex, it does not necessarily follow that relative variability obeys the same rule. In order to determine the degree of relative variability in vital capacity at different ages, and for each sex, it is necessary to resort to methods of statistical analysis of the data. This is attempted in a succeeding paragraph.

TABLE 1.—NORMAL BOYS. AGE, NUMBER OF CASES, AVERAGE STANDING HEIGHT, AVERAGE AND RANGE OF VITAL CAPACITY, MEAN VITAL CAPACITY DETERMINED BY GRAPHIC INTERPOLATION, ABSOLUTE AND PERCENTAGE ANNUAL INCREASE IN VITAL CAPACITY, FORMULA FOR COMPUTING VITAL CAPACITY FROM AGE WITH VALUE OBTAINED BY USE OF FORMULA, PROBABLE ERROR, STANDARD DEVIATION, AND COEFFICIENT OF VARIATION

Age in Years	No. of Cases	Standing Height, Cm.	Average Vital Capacity, C.c.	Minimum Vital Capacity, C.c.	Maximum Vital Capacity, C.c.	Mean V. C. Determined by Graphic Interpolation, C.c.	Absolute Annual Increase in V. C., C.c.	Percentage Yearly Increase in Vital Capacity	V. C. as Computed by Formula y = (ax) ± b C.c.	Empirical Formula and Values for Constants Used for Each Age Group y = (ax) ± b	Probable Error of Random Sampling, C.c.	Standard Deviation, C.c.	Coefficient of Variation, per Cent.
4	6	103.4	792	500	900	792	...	....	791	y = V. C.			
5	20	106.8	927	600	1,150	958	166	21.0	969	a = Age in years			
6	62	112.2	1,154	800	1,600	1,124	166	17.3	1,146	x = 177.5	15.6	182	15.8
7	112	116.9	1,290	900	2,200	1,304	180	16.0	1,323	b = +81	12.3	194	15.0
8	98	121.8	1,468	1,060	2,100	1,491	187	14.3	1,501		15.0	220	15.0
9	110	129.9	1,715	1,200	2,300	1,679	188	2.6	1,679		15.8	246	14.3
10	87	133.4	1,872	1,400	2,650	1,859	180	10.7	1,856	y = V. C.	18.9	262	14.0
11	113	137.8	1,991	1,300	2,800	2,015	156	8.2	2,034	a = Age in years	17.1	270	13.6
12	114	142.4	2,182	1,300	3,300	2,210	195	9.0	2,212	x = 178.0 b = +76	21.5	340	15.6
13	132	148.7	2,458	1,700	4,000	2,451	241	10.9	2,450	y = V. C.	25.2	430	17.5
14	177	154.8	2,712	1,400	4,300	2,772	321	13.1	2,760	a = Age in years	24.5	484	17.8
15	155	159.9	3,145	1,850	4,400	3,094	322	11.6	3,070	x = 310.0	29.8	551	17.5
16	67	167.2	3,425	2,100	4,300	3,417	323	10.8	3,380	b = −1,580	47.2	573	16.7
17	23	171.4	3,776	2,400	4,500	3,708	289	8.5	3,690				
18	9	172.0	3,922	2,750	4,400	3,999	281	7.6	4,000				
19	4	168.2	4,300	4,100	4,500	4,300	301	7.5	4,310				

TABLE 2.—NORMAL GIRLS. AGE, NUMBER OF CASES, AVERAGE STANDING HEIGHT, AVERAGE AND RANGE OF VITAL CAPACITY, MEAN VITAL CAPACITY DETERMINED BY GRAPHIC INTERPOLATION, ABSOLUTE AND PERCENTAGE ANNUAL INCREASE IN VITAL CAPACITY, FORMULA FOR COMPUTING VITAL CAPACITY FROM AGE WITH VALUES OBTAINED BY USE OF FORMULA, PROBABLE ERROR, STANDARD DEVIATION, AND COEFFICIENT OF VARIATION

Age in Years	No. of Cases	Standing Height. Cm.	Average Vital Capacity, C.c.	Minimum Vital Capacity, C.c.	Maximum Vital Capacity, C.c.	Mean V. C. Determined by Graphic Interpolation, C.c.	Absolute Annual Increase in V. C., C.c.	Percentage Yearly Increase in Vital Capacity	V. C. as Computed by Formula $y=(ax)\pm b$ C.c.	Empirical Formula and Values for Constants Used for Each Age Group $y=(ax)\pm b$	Probable Error of Random Sampling, C.c.	Standard Deviation, C.c.	Coefficient of Variation, per Cent.
4	9	95.4	664	350	850	644	...	....	644	y = V. C. in Cm. a = Age in years x = 175.3 b = —57			
5	26	106.4	888	600	1,200	852	208	32.3	819				
6	62	111.5	1,085	700	1,600	1,045	193	22.7	995		14.0	163	15.0
7	81	114.4	1,228	900	1,800	1,215	170	16.3	1,170		13.6	181	14.7
8	76	121.0	1,401	800	1,950	1,373	158	13.0	1,345		15.4	199	13.5
9	73	127.0	1,513	1,000	2,250	1,524	151	11.0	1,521		18.1	229	15.1
10	117	132.1	1,672	900	2,400	1,685	161	10.6	1,696		17.0	273	16.3
11	119	135.9	1,799	1,250	2,550	1,871	186	11.0	1,871		14.9	241	13.4
12	135	141.0	2.053	1,400	2,900	2 085	214	11.4	2.085	y = V. C. in Cm. a = Age in years x = 183.0 b = —111	19.9	343	16.7
13	162	151.4	2,349	1,550	3,600	2,309	224	10.7	2,268		21.7	409	17.5
14	192	156.6	2,607	1,900	3,800	2,511	202	8.7	2,451		17.5	361	13.9
15	131	157.8	2,702	1,900	3,700	2,676	165	6.6	2,634		24.3	413	15.3
16	29	160.1	2,778	2,050	3,500	2,817	141	5.3	2,817				
17	7	162.6	2,943	2,250	3,400	2 955	138	4.9	2 958	y = V. C. in Cm. a = Age in years x = 141.2 b = +558			
18	1	162.0	3,100	.....	.....	3,100	145	4.9	3,100				

The general trend of the increase in the average vital capacity of the lungs with advancing age is shown graphically in Figure 1. In order to eliminate minor fluctuations the curves have been smoothed by means of graphic interpolation. This produces a curve which probably conforms more exactly with the type of curve that would be obtained from averages based upon an infinitely large number of cases, and probably represents more nearly the true mean vital capacity. The mean vital capacity at each age, as determined by graphic interpolation, is recorded in Tables 1 and 2, and represented in graphic form in Figure 1. The actual averages for the vital capacity are represented in the figure by dots for the boys and by circles for the girls. In general, the smoothed curve of vital capacity for each sex tends to assume a concave form corresponding closely with the curve based on the actual averages. From 4 to 11 years, inclusive, the curve for boys is practically a straight line, due to the fair uniformity of the yearly increase in vital capacity. This is followed later by a period of acceleration reaching a maximum at 14 years, which apparently is fairly well maintained, although at a reduced rate, at least until 19. This accounts largely for the general concavity of the curve.

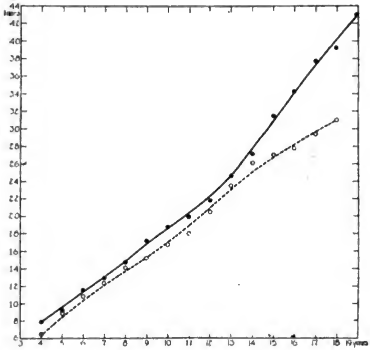

Fig. 1.—Showing smoothed curves representing the average absolute increase in the vital capacity of the lungs as determined by graphic interpolation, for boys between 4 and 19 years of age inclusive, and for girls between 4 and 18 years of age inclusive. The actual averages at each age for the boys are represented by dots and by circles for the girls. Vital capacity in liters is represented on the ordinate, and age in years on the abscissa. The solid line represents the boys; the broken line the girls in this and Figures 2, 3 and 4.

There appear, therefore, to be three main phases in the curve representing the increase in vital capacity for the boys between 4 and 19 years: (1) a period of fairly uniform increase between 4 and 10; (2) a period of acceleration extending from 12 to 14, and (3) a period of uniform but less rapid increase in vital capacity to 19.

The smoothed curve of vital capacity (Fig. 1) for the girls likewise shows several phases. Between 4 and 6 years of age the curve rises rather abruptly. From 7 to 10 the annual increase in vital capacity is fairly uniform but slower than during the earlier period. An acceleration in the rate of increase occurs at 11 and persists until 13. Due, in part, to the failure of this rapid yearly increase in vital capacity to continue during the following five years, the concavity produced by the prepubertal acceleration in the curve of vital capacity as plotted against age is much less marked for the girls than for the boys, and also does not extend over as great a period of years as with the former.

The accelerated increase in vital capacity appearing at 11 and 12 years of age for the girls and boys, respectively, is, no doubt, related to the normal prepubertal acceleration of the growth of the body as a whole.

The difference in vital capacity between girls and boys at corresponding ages, is clearly shown by the curves in Figure 1. Throughout the period studied the boys have the larger lung capacity. At 6 years the difference amounts to approximately 79 c.c., which at 10 years has increased to 174 c.c. Subsequently the girls show a more rapid increase in vital capacity which reduces the difference to 125 c.c. at 12 years of age. From the fourteenth year on, the difference in vital capacity between the two sexes, rapidly increases.

As long ago as 1854 Wintrich[2] noted the existence of a sexual difference in the vital capacity of the lungs, and observed that this difference persists until old age. Since then this observation has been confirmed frequently by practically all investigators who have studied the subject. Among the more recent and extensive observations on children, the data collected by Gilbert,[3] for 1,279 boys and 1,244 girls, and also Smedley's[4] averages for 2,788 boys and 3,471 girls, show the vital capacity at all ages to be larger for the boys. Baldwin[5] apparently is the only one who has obtained different results. He states that boys have a greater lung capacity on the average than the girls, except between 13 and 14 years of age when just the reverse is true. My own data indicate a larger vital capacity for the boys at all ages, and thus are in agreement with the findings of Gilbert, Smedley and others.

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[2] Wintrich, M. A.: Einteilung zur Darstellung der Krankheiten der Respirations organe. Virchow, R.: Handbuch der speciellen Pathologie u. Therap. **92,** 1854.

[3] Gilbert, J. A.: Researches on the Mental and Physical Development of School Children. Studies from Yale Psychological Laboratory, **2,** 1894. Researches on School Children and College Students. University of Iowa Studies in Psychology. **1,** 1897.

[4] Smedley, F. W.: Report of Commissioner of Education **1,** 1902.

[5] Baldwin, B. T.: Physical Growth and School Progress, U. S. Bureau of Education Bull. No. 10. The Normal Child. Its Physical Growth and Mental Development, Pop. Sc. Monthly **85,** 1914.

The absolute yearly increase in vital capacity for the boys (Table 1) is fairly uniform until 10 years of age, but at the eleventh year the increase is considerably lower than that registered at any other time. Following this period of retardation, the absolute annual growth in vital capacity becomes accelerated and until 19 years maintains a more rapid rise than occurs at any earlier age.

With the girls the average absolute annual increase in vital capacity (Table 2) also is fairly uniform between 6 and 10 years of age. Starting at 11 years (one year earlier than noted with the boys), the absolute annual increase becomes accelerated, but is maintained only until the fifteenth year; whereas with the boys the vital capacity continues to grow rapidly until 19 years of age. This results on a marked divergence at the period between the curves for vital capacity for the two sexes when plotted against age. The greatest annual gain in vital capacity amounted to 323 c.c. for the boys during the fifteenth year, as compared with a smaller maximum of 224 c.c. for the girls at 13 years of age.

A consideration of the percentage annual increase in vital capacity gives one a conception of the relative rapidity of growth in this respect at different ages. With the boys the rate of relative increase diminishes rapidly from an average annual gain between 4 and 5 years of 21 per cent., to a minimum rate of 8.2 per cent. at 11 years of age. During the following three years, the rate of growth of lung capacity becomes relatively more rapid, rising to 13.1 per cent. at 14 years, but later steadily declines.

With the girls the relative increase in vital capacity decreases from 32.3 to 10.6 per cent. between 5 and 10 years inclusive. During the following two years the rate of annual growth becomes more rapid, amounting to 11.4 per cent. at 12 years as compared with a rise to 13.1 per cent. for the boys at 14. Following this period of acceleration, the rate of increase in lung capacity diminishes rapidly.

In general, then, for each sex the relative rate of annual growth in vital capacity shows a tendency to decrease during early childhood, becomes slightly more rapid about the time of the advent of puberty, and later gradually declines. The period of acceleration in the rate of lung capacity growth begins and terminates at an earlier age with the girls than with the boys.

The data published by Smedley,[4] which are the most extensive series of observations on children at present available in the literature, likewise show that the rate of annual increase in vital capacity diminishes during early childhood, rises about the time of puberty and later declines. His averages also indicate that the prepubertal acceleration appears later, and is relatively greater with the boys than with the girls.

If we now return to a consideration of the smoothed curves of vital capacity as plotted against age (Fig. 1) it is found possible to divide the curve for each sex into three phases, so selected that each segment conforms closely to straight lines of different incliniation. Thus for the boys the portions of the curve between 4 and 9 years, between 10 and 12 years, and between 13 and 19 years deviate but slightly from the straight lines connecting these various points. Likewise, with the girls the successive segments from 4 to 11, 12 to 14, and 15 to 18 years of age, inclusive, also conform rather closely to the different straight lines drawn through these points.

The value of any point upon a straight line may be readily determined by means of the empirical formula $y = ax \pm b$, where $y =$ the unknown value, $a =$ a known variable, $x =$ a constant, and $b =$ a second constant. It follows, therefore, that the vital capacity between successive segments of the curve conforming closely to a straight line may be determined in a fairly satisfactory and accurate manner by employing the above formula where $y =$ the vital capacity to c.c., $a =$ the age in years, $x =$ a constant, and $\pm b =$ a second constant. The vital capacity as derived by formula, and also the different values for the constants x and b are given in Tables 1 and 2. On inspecting the data the computed vital capacities are found to agree rather closely with the means as determined by graphic interpolation. With the boys the greatest difference occurs at 16 years where value derived by formula is 37 c.c. too low. For the girls the greatest deviation amounts to 60 c.c. at 14 years. Evidently, therefore, the vital capacity of the lungs for each between certain ages, may be derived with fair accuracy by means of a simple straight line formula.

The necessity of establishing some relationship between the vital capacity of the lungs and other body measurements in order to be of any practical clinical value has long been recognized. In 1846 Hutchinson,[6] by inventing the spirometer, was the first to obtain extensive and accurate records of vital capacity. From this scientific pioneer study Hutchinson concluded that a definite relationship exists to standing height, the vital capacity increasing in a simple arithmetical progression with increase in height. For each additional inch with individuals between 5 and 6 feet tall he states that 8 additional cubic inches of air at 60 F. may be given out by a forced expiration. Hutchinson also recognized that weight, age and sex might modify averages to some extent, but believed, however, that no definite relationship existed between vital capacity and either the body weight, the sitting height, or the chest circumference.

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[6] Hutchinson, J.: On the Capacity of the Lungs and on the Respiratory Functions, Med. chir. Tr. **29**, 1846, Lancet **1** 1846.

Fabius[7] pointed out the occurrence of marked individual variation from averages based on height. He asserted that the vital capacity divided by the product of of the stem length (measured from the external accipital protuberance to the tip of the coccyx) and the chest circumference produced a constant which varied only a slight extent with different individuals. The cause of this variability in the constant Fabius attributed to differences in age and chest expansion. Fabius emphasized, therefore, that the length, circumference and mobility of the chest should be measured in determining whether or not an individual's vital capacity is normal.

Wintrich[2] investigated the vital capacity of the lungs of 3,500 healthy persons including 500 women. He noted that during childhood age influenced the vital capacity markedly, and also that a sexual difference persisted into old age. Wintrich was interested mainly in the relationship between vital capacity and height.

Schneevoogt[8] concluded that standards of vital capacity in relation to age and height are of the most practical value, and claimed that deviations of 500 c.c. from such standards could not be assumed to be necessarily abnormal.

Arnold[9] found extremes of fluctuations to be greater when comparisons were made on a basis of stem length, rather than on standing height. In discussing the smaller vital capacity of the lungs of women as compared with the men relative to height and chest circumference, Arnold points out that the chest expansion is less for the females than for the males.

From a study of the vital capacity of the lungs of 515 students, Kottelman[10] observed that the lung capacity increases with age faster than the growth in body length occurs. MacDonald[11] points out that the data presented by Kottelman also show that weight increases with age more rapidly than increase in lung capacity.

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[7] Fabius, H.: De spirometro ejusque usu observationibus cum alioum, tum propriis illustrato, Diss. Amsterdam, Ztschr. rationell. Med. **4,** 1853.

[8] Schneevoogt, G. E. V.: Ztschr. rationelle med. **9,** 1854, (cited by Lungsgaard and Van Slyke).

[9] Arnold, F.: Ueber die Athmungsgrösse des Menschen, Heidelberg, 1855.

[10] Kottelman, L.: Die Körper verhält nisse der gelehrten Schüler des Johannaens in Hamburg, Ztschr. d. Königlch Preussischen statistischen Bureaus, Berlin, 1879.

[11] Mac Donald, A.: Experimental Study of Children, U. S. Bureau of Education Report of Commisioner **1,** 1897.

The existence of a relationship between vital capacity and weight is disputed by Hall.[12] This observer arrived at the unique conclusion that the vital capacity varies directly with the strength of the individual.

Bohr[13] objected to the use of standing height for estimating the normal vital capacity on the grounds that the individual variability is so great as to render this method inapplicable. He maintained that the total and residual air as well as the vital capacity should be determined, and placed greater emphasis upon the percentage relationship between these various subdivisions of the total lung volume, than on their absolute value. Hasselbach,[13a] Rubow,[14] Siebeck,[15] Bie and Maar[16] and Plesch[17] also investigated the relationship between the total lung volume, the middle and vital capacities and the residual air in normal and pathologic conditions, and likewise were interested more in the relative than in the absolute value of the different volumes.

Peabody and Wentworth,[18] studying the vital capacities for a group of 140 healthy adults (ninety-six males and forty-four females), divided the subjects into three groups according to their height and considered the average vital capacity for each group as a normal standard for corresponding height. Of the ninety-six men, 84 per cent. registered vital capacities falling within 10 per cent. of their respective normal. These same authors, in a study of a small group of cases, have also found a rather close relationship to the body surface area.

Recently Lundsgaard and Van Slyke[19] have claimed that the vital capacity of the lungs is closely related to the calculated chest volume.

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[12] Hall, W. S.: Changes in the Proportions of the Human Body During the Period of Growth, J. Authropol. Inst. of Great Britain and Ireland **25,** 1896.

[13] Bohr, C.: Die funktionellen Aenderungen in der Mittellage und Vital Kapazität der Lungen, Deutsch. Arch. f. klin. Med. **88,** 1906.

[13a] Hasselbach, K. A.: Ueber die Einwinkung der Temperatur auf die vitale Mittelage der Lungen. Ueber die Total Kapazität der Lungen, Deutsch. Arch. f. klin. med. **93,** 1908.

[14] Rubow, V.: Untersuchungen über die Atmung bei Herzkrankheiten; ein Beitrag zum Studium der Pathologie des kleinen Kreuslaufes, Deutsch. Arch. f. Klin. Med. **92,** 1908.

[15] Siebeck, R.: Ueber die Beinflussung der Atemmechanik durch krankhafte Zustande des Respirations und Kreislaufapparates, Deutsch. Arch. f. klin. Med. **100,** 1910.

[16] Bie, W., and Marr, W.: Dem Fall von angeborenem Herzfehler mit Cyanose und Polyglobulie, Deutsch. Arch. f. klin. Med. **99,** 1910.

[17] Plesch, J.: Die pathologische Physiologie des Lungen volumens und seine Beziehung zum Kreislauf, Ztschr. f. Exper. Path. u. Therap. **13:** 1913.

[18] Peabody, F. W., and Wentworth, J. A.: Clinical Studies on Respiration. IV. The Vital Capacity of the Lungs and Its Relation to Dyspnea, Arch. Int. Med. **20:**468 (Sept.) 1917. Peabody, F. W.: Cardiac Dyspnea, Am. J. M. Sc. **155:**100, 1918.

[19] Lundsgaard, C., and Van Slyke, D. D.: Studies of Lung Volume 1. Relation Between Thorax Size and Lung Volume in Normal Adults, J. Exper. M. **27:**651, 1918.

The chest they considered as a geometrical figure and the product of three dimensions was considered to represent a volume proportional to the chest volume. The height of the chest was taken as the length of the sternum from the superior border to a point just below the articulation with the xiphoid cartilage. The depth was taken as the horizontal distance from the middle of the sternum at the level of the insertion of the third costal cartilage, to the spinal column; and the breadth as the distance across the sixth rib in the mid axillary line.

The normal vital capacity in man and its relation to the size of the body has also been the subject of a paper published recently by Dreyer.[20] Based largely on the data of Hutchinson[6] and Schuster,[21] together with some observations of his own, Dreyer has claimed that the vital capacity is a function of the weight. This, he says, can be expressed by the formula $\frac{W^n}{v.c.} = K$, where W is the net weight in grams, v.c. the vital capacity in cubic centimeters, the power n is 0.72, and K is a constant. He further states that since it is already established that $\frac{W^n}{S} = K_2$ where W = net weight, S = body surface and n is 0.72, it follows that the vital capacity is a simple function of the body surface.

The relation between the vital capacity and stem length Dreyer finds to be correctly expressed by the formula $\frac{SH^n}{v.c.} = K_3$ where SH = the stem length in centimeters, v.c. = vital capacity in cubic centimeters, the power n is approximately 2, and K_3 is a constant. Between the vital capacity and the chest circumference the existing relation can be expressed by the formula $\frac{Ch^n}{v.c.} = K_4$, where Ch = circumference of chest in cubic centimeters, v.c. = the vital capacity in centimeters, the power n is approximately 2, and K_4 is a constant.

Also $\frac{SH \times Ch}{v.c.} = K_5$ where SH stem length in centimeters Ch = chest circumference in centimeters v.c. = vital capacity in cubic centimeters, and K_5 is a constant. Dreyer has pointed out, therefore, that the vital capacity is definitely related to the 0.72 power of the weight, directly to the body surface area, to the square of the stem length, to the square of the chest circumference, and to the trunk volume (estimated as the product of the chest circumference and stem length), and states that the above is also the order of the importance of these relations.

In discussing the variability of vital capacity in normal persons, Dreyer shows that for the 16 individuals which he studied the mean deviation, as estimated by the method of least squares, of the values

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20. Dreyer, G.: Investigations on the Normal Vital Capacity in Man and its Relation to the Size of the Body, Lancet **2**:227, 1919. Dreyer, G., and Burrell, L. S. T.: The Vital Capacity Constants Applied to the Study of Pulmonary Tuberculosis, Lancet **1**:1212, 1920.

21. Schuster, E.: First results from the Oxford Authropometric Laboratory, Biometrika **8**, 1911.

for K computed from the formula based on the two thirds and the 0.72 power of the body weight, in the two cases amounted to 3.56 and 2.64 per cent., respectively, or distinctly lower when the best power for the weight (0.72) is used. This, Dreyer says, indicates that if a person is found to have a vital capacity 6 per cent. smaller or larger than that calculated from his body surface, he probably has a normal vital capacity, and if the vital capacity is 10 per cent. above or below the normal it is almost certain to be abnormal. On using the data of Fitzgerald, Purefoy and Haldane,[22] however, a mean deviation of 15.8 per cent. is obtained, or five times as great as in Dreyer's series. Dreyer attributes this great difference in variability to the fact that the observations of Fitzgerald, Purefoy and Haldane were carried out on a more highly mixed material. He also calls attention to the differences in vital capacity exhibited by the different classes studied by Hutchinson, which apparently have nothing to do with fundamental bodily deficiencies but are simply a result of conditions depending upon occupation and mode of life.

The existence of normal individual difference of vital capacity has constituted a real difficulty in its practical clinical application, but aside from this study of Dreyer's, apparently no one has attempted to estimate its extent by statistical methods. It is absolutely essential to determine the magnitude of the deviation from the average met with in normal and healthy individuals, before it is possible to decide whether the vital capacity for any given person should be considered normal or abnormal. Knowing the extent of normal variability of vital capacity also enables one to more fully appreciate both the limitations and the possibilities of its applicability in clinical work. In this study an attempt is made to determine the extent of variability of vital capacity during childhood.

Before entering into a consideration of the normal variability, a consideration of the reliability of the averages obtained for the vital capacity seems appropriate. The measure of the trustworthiness of an average derived from a limited number of observations is furnished by the so-called probable error of random sampling. To be more explicit, the probable error of random sampling is a measure of the extent that the average values would be expected to vary, were the observations made at random upon an infinitely large number of comparable series of cases, and is so chosen, that half of these values would lie inside, and half outside the limits of the probable error. Therefore in an infinitely large series roughly 50 per cent. of the averages will fall within the limit of the range of the probable error about the average based upon a limited number of cases. The probable error assumes the data to be technically correct, and has nothing to do with inaccuracies in measurement. The probable error of the average or mean vital capacity at each age has been calculated by means of the formula $0.6745 \times \frac{S}{\sqrt{n}}$ where S = standard deviation, and n = number of observations, and the results obtained may be found in Tables 1 and 2. The derivation and significance of the standard deviation is discussed at a later time.

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[22] Fitzgerald, Purefoy, M., and Haldane, J. S.: The Normal Alveolar Carbonic Acid Pressure in Man, J. Physiol. **32,** 1905.

During childhood it appears that in general, for the various groups, the calculated probable error of random sampling for each sex (Tables 1 and 2) constantly increases with advancing age. For the boys the value 15.6 c.c. at 6 years has increased to 29.8 c.c. at 15 years of age. With the girls during this same period the probable error increases from 14 at 6 to 24.3 at 15 years. In applying this information we can conclude for the boys at 15 years of age, that were the vital capacity taken for a large series of comparable groups of individuals the chances are that half these series would show averages falling between 3,145 c.c. ± 29.8 c.c., while the remaining 50 per cent. lie either above or below this limit. In other words, for boys at this age, 50 per cent. of all group averages can be expected to vary not more than 29.8 c.c. above or 29.8 c.c. below that obtained. Derivations markedly beyond these limits probably indicate the existence of biological differences between the groups concerned.

The most commonly used measure of the dispersal of the individual measurements from the average of the sum of all the observations is the standard deviation. The standard deviation is obtained first by squaring all the deviations from the average, summing these squares, and then dividing this sum by the number of deviants, which gives the mean-square deviation. The square root of this mean-square deviation is designated as the standard deviation. The practical value of the standard deviation lies in the fact that it indicates the degree of the absolute variability, within the limits of which the probability is that the measurement obtained is more apt to be normal, and commonly the greater the deviation beyond the limits established by the standard deviation the greater the probability is that the measurement is abnormal. It is also particularly useful in the determination of measures of interrelationship.

The standard deviation from the average vital capacity of the lungs at each age has been calculated for the boys between 6 to 16 years, inclusive, and from 6 to 15 years for the girls (Tables 1 and 2). The number of subjects in each group during this period was considered sufficiently large to justify the procedure. Between 6 and 16 years of age for both sexes the absolute value of the standard deviation increases roughly three fold. With the boys it increases from about 182 c.c. at

6 years to 573 c.c. at 16 years. If we attempt to apply this information in considering whether or not any single observation falls within normal limits, then at 16 years of age the vital capacity in individual cases might vary 573 c.c. either above or below the average value of 3,425 c.c. at this age, and could not be considered as definitely abnormal. In clinical work, however, those subjects approaching the lower limits of normal variability would, no doubt, cause the greater concern.

With the girls the standard deviation (Table 2) increases from 163 c.c. at 6 years to 413 c.c. at 15 years. At corresponding ages the absolute value of the standard deviations are usually somewhat smaller for the girls than for the boys.

In order to make comparison between the relative degree of variability of the vital capacity at different ages, it is necessary to reduce the various standard deviations to a comparable basis. This is readily accomplished by computing the percentage that the standard deviation at each age forms of the average vital capacity for that period. This relative variability constant is known as the coefficient of variation, and is in reality the per cent. that the standard deviation forms of the respective mean or average.

For the boys the coefficient of variation (Table 1) between 6 and 11 years of age apparently decreases from 15.8 to 13.6. Thus at 6 years the normal variability of vital capacity expected is approximately 15.8 per cent. above or below the average for that age, which at 11 years has decreased to 13.6 per cent. During the following years the vital capacity becomes considerably more variable, the coefficient of variation at 14 years rising to 17.8, with apparently a tendency to decrease during the succeeding two years.

For the girls the coefficient of variation (Table 2) decreases from 15 at 6 years to 13.5 at 8 years. Subsequently it rises; reaching a maximum of 17.5 at 13 years, one year earlier than the maximum coefficient of variation recorded for the boys. Later the variability apparently decreases. At 11 years of age an unusually low coefficient of 13.4 was obtained from the data, which possibly may be accidental in character. On consideration of the extent of variability in vital capacity it appears that for each sex variability decreases during early childhood, increases about the period of puberty, and later declines. In the main essentials the general trend of the variability in vital capacity is quite similar to that noted in respect to variability in weight and height during growth, for similarly the variability of these two physical measurements decreases at first, rises to attain a maximum about the time of puberty, and then diminishes again.

Although the standard deviation and the coefficient of variation gives a rough measure of the degree of absolute variability, a further conception of variability may be gained through the determination of the probable error of the data. Provided the curve of distribution of the individual observations conforms to the ideal mathematical type of symmetrical distribution curve, the statistical constant known as the probable error of the data establishes limits within which approximately 50 per cent. of all observations taken at random will be expected to fall. Of the remaining 50 per cent. of observations, 25 per cent. will lie above and 25 per cent. below the limits established. The probable error of the data may be computed by means of the formula 0.6745 × SD, where SD is the standard deviation. In general, if a large number of observations is collected, one finds that the majority occur near the average value for the measurement taken, and the greater the deviation from the average the smaller the groups become. The frequency or distribution curve plotted for extensive series of observations often is found to conform very closely to the ideal symmetrical mathematical type of distribution or probability curve. Under such circumstances the determination of the probable error of the data of this series of observations is of especial significance as explained above. With respect to the observations on the vital capacity of the lungs the value and significance of the distribution curves based upon this data is greatly limited due to the small number of observations available. The data at present are insufficient to establish definitely the character of their distribution curve. At some later time it is hoped to be able to accumulate enough data to definitely establish an approximate limiting distribution curve for this measurement. To date, however, the curves obtained for the vital capacity in general appear to conform fairly well with the ideal symmetrical mathematical distribution curve. For the present, therefore, I feel it safe to assume that approximately 50 per cent. of cases taken at random will have vital capacities falling within the limits established by the probable error of the standard deviation for the group concerned. Twenty-five per cent. will lie above and 25 per cent. below these limits. If expressed in terms of per cent., the children constituting the last group, in general, have vital capacities 10 per cent. or more below the expected normal. By recording any individual vital capacity, one thus may easily classify the patient as to the group to which the child belongs. Subjects falling into the group representing the poorer one fourth of the child population are children who probably deserve special study to eliminate pulmonary or cardiac disease as a factor causing their low standard of physical fitness. Experience has shown, however, that an apparently normal vital capacity does not exclude the necessity of thorough examination when the patient is suspected of having tuberculosis, for occasionally the vital capacity may be normal as compared with averages, even in the presence of serious disease of the lungs. Should the accumulation of more extensive observation on the vital capacity of the lungs reveal the fact that the frequency curve derived from such data does not conform to the ideal symmetrical mathematical probability curve, but shows a certain definite skewness the above statements necessarily must be modified.

3. *Vital Capacity and Standing Height.*—In Tables 3 and 4 the data have been averaged in groups (sexes separated), each group including subjects differing 5 cm. or less in standing height, age and other physical measurement being disregarded. With a growth from an average of 108 cm. to 168 cm. in height, the vital capacity for the boys (Table 4) has increased from 1,074 c.c. to 3,625 c.c., an increase of 2,551 c.c. Thus, with an increase of 60 cm. in standing height representing approximately 54.5 per cent. growth of this measurement, the vital capacity has increased more than 237 per cent. On the whole, then, growth of vital capacity at this period with the boys, occurs about four times as rapidly as the growth in height.

For the girls, accompanying a growth in height from 108 cm. to 168 cm. the vital capacity (Table 4) increases from 1,022 c.c. to 3,017 c.c. This increase of 1,995 c.c. represents a percentage increase of about 195 per cent., as compared with 237 per cent. with the boys for a corresponding growth in height. Nevertheless, also with the girls the lung capacity increases more rapidly than increase in height occurs.

The increase in lung capacity for each sex as plotted against standing height is represented graphically by means of smoothed curves (as determined by graphic interpolation) in Figure 2. The curves for each sex when determined by this method tend to pursue a sinuous course, being somewhat concave in form with the boys up until the standing height reaches approximately 175 cm., and with the girls until they become about 165 cm. tall. Beyond these points the direction of each curve changes tending to straighten out to some extent. The greater vital capacity for the boys as compared with the girls of corresponding height is clearly shown. The extent of the difference between the boys and girls in general appears to increase constantly as they grow taller. If we analyze the curves more completely we find that with the boys the increase in vital capacity plotted against height, is fairly uniform until the individuals are about 148 cm. tall. With growth from 148 cm. to 173 cm. in height, the increase in vital capacity becomes more rapid, but beyond 173 cm. it diminishes considerably in rate.

For the girls the most rapid increase in vital capacity accompanies the growth in height from 143 to 160 cm.

The absolute increase in vital capacity (Tables 3 and 4) which accompanies each successive growth of 5 cm. in standing height is fairly uniform with the boys until they become approximately 143 cm. tall and with the girls until they reach a standing height of 138 cm. At

TABLE 3.—NORMAL BOYS. NUMBER OF CASES, AVERAGE STANDING HEIGHT, AVERAGE VITAL CAPACITY, MEAN VITAL CAPACITY AS DETERMINED BY GRAPHIC INTERPOLATION, ABSOLUTE AND PERCENTAGE INCREASE IN VITAL CAPACITY ACCOMPANYING EACH 5 CM. GROWTH IN HEIGHT, VITAL CAPACITY AS COMPUTED FROM HEIGHT BY FORMULA FOR EACH HEIGHT GROUP, PROBABLE ERROR, STANDARD DEVIATION, AND COEFFICIENT OF VARIATION

Number of Cases	Standing Height, Cm.	Average Vital Capacity, C.c.	Mean V. C. Determined by Graphic Interpolation, C.c.	Absolute Increase in Vital Capacity, C.c.	Percentage Increase in Vital Capacity, C.c.	Vital Capacity as Computed by Formula y = (ax) ± b	Empirical Formula for Each Height Group y = (ax) ± b	Probable Error of Random Sampling, C.c.	Standard Deviation, C.c.	Coefficient of Variation, per Cent.
3	98	837	837	...	....	838	y = V. C.			
6	103	788	912	75	9.0	963	a = Height in Cm.			
40	108	1,074	1,062	150	16.4	1,069	x = 25.1	15.0	140	13.0
83	113	1,190	1,194	132	12.4	1,214	b = —1,622	11.0	149	12.5
84	118	1,332	1,340	146	12.2	1,340		11.1	151	11.8
89	123	1,474	1,500	160	11.9	1,499	y = V. C.	12.6	176	11.9
96	128	1,690	1,674	174	11.6	1,684	a = Height in Cm.	13.6	197	11.7
109	133	1,828	1,853	179	10.7	1,869	x = 37	12.2	188	10.3
118	138	2,050	2,034	181	9.8	2,054	b = —3,662	14.0	227	11.1
123	143	2,230	2,220	186	9.1	2,239		15.5	255	11.4
114	148	2,359	2,423	203	9.1	2,424		15.6	278	11.8
97	153	2,594	2,660	237	9.8	2,659	y = V. C.	18.1	264	10.2
115	158	2,936	2,935	255	9.5	2,948	a = Height in Cm.	22.4	357	12.2
75	163	3,173	3,243	308	10.5	3,237	x = 57.8	29.1	373	11.7
77	168	3,625	3,547	304	9.4	3,526	b = —6,181	31.7	413	11.5
35	173	3,919	3,815	268	7.6	3,815				
16	178	4,094	4,020	205	5.4	4,020	y = V. C.			
3	183	4,167	4,175	155	3.9	4,160	a = Height in Cm			
1	188	4,300	4,300	125	3.0	4,300	x = 28 b = —964			

TABLE 4.—NORMAL GIRLS. NUMBER OF CASES, AVERAGE STANDING HEIGHT, AVERAGE VITAL CAPACITY, MEAN VITAL CAPACITY AS DETERMINED BY GRAPHIC INTERPOLATION, ABSOLUTE AND PERCENTAGE INCREASE IN VITAL CAPACITY ACCOMPANYING EACH 5 CM. GROWTH IN HEIGHT, VITAL CAPACITY AS COMPUTED FROM HEIGHT BY FORMULA, FORMULA FOR EACH HEIGHT GROUP, PROBABLE ERROR, STANDARD DEVIATION, AND COEFFICIENT OF VARIATION

Number of Cases	Standing Height, Cm.	Average Vital Capacity, C.c.	Mean V. C. Determined by Graphic Interpolation, C.c.	Absolute Increase in Vital Capacity, C.c.	Percentage Increase in Vital Capacity with 5 Cm. Growth in Length, C.c.	Vital Capacity as Computed by Formula $y = (ax) \pm b$	Empirical Formula for Each Height Group $y = (ax) \pm b$	Probable Error of Random Sampling, C.c.	Standard Deviation, C.c.	Coefficient of Variation, per Cent.
5	98	755	755	...	....	755	(25.5 × Ht.) — 1,744 = V. C.			
20	103	851	876	121	16.0	882				
37	108	1,022	1,005	129	14.7	1,010				
68	113	1,118	1,136	131	13.0	1,137		11.9	146	13.1
71	118	1,283	1,276	140	12.3	1,276	(29.5 × Ht.) — 2,205 = V. C.	12.2	153	11.9
86	123	1,412	1,414	138	10.8	1,423		10.6	146	10.3
85	128	1,555	1,560	146	10.3	1,571		12.7	173	11.1
93	133	1,698	1,707	147	9.4	1,718		12.9	185	10.9
104	138	1,870	1,865	158	9.3	1,866		13.4	208	10.9
109	143	2,005	2,086	171	9.2	2,036	(39.7 × Ht.) — 3,641 = V. C.	14.8	229	11.4
98	148	2,211	2,230	194	9.5	2,234		17.3	254	11.5
164	153	2,449	2,439	209	9.4	2,432		16.4	312	12.7
141	158	2,661	2,646	207	8.5	2,631		18.6	328	12.3
96	163	2,855	2,830	184	7.0	2,830		22.8	332	11.6
35	168	3,017	2,978	148	5.2	2,978	(24.3 × Ht.) — 1,104 = C. C.			
3	173	3,100	3,100	122	4.1	3,100				

these points the absolute increase rises rapidly reaching a maximum of 308 c.c. for the boys when 163 cm. tall, as compared with 209 c.c. for the girls at a standing height of 153 cm. Subsequently the absolute increase for each sex steadily declines. Evidently, therefore, with each sex the increase in vital capacity for each 5 cm. growth in height is not uniform throughout childhood. Hutchinson's conclusion, based on data collected largely from adults, that vital capacity increases in a simple arithmetical progression with increasing height certainly does not apply to the period of childhood. Dreyer has demonstrated recently from Hutchinson's data that this contention was erroneous, and has shown that even for adults the vital capacity is not a simple function of the body height, since it increases in an irregular manner and not at a fixed rate with each unit increase in height.

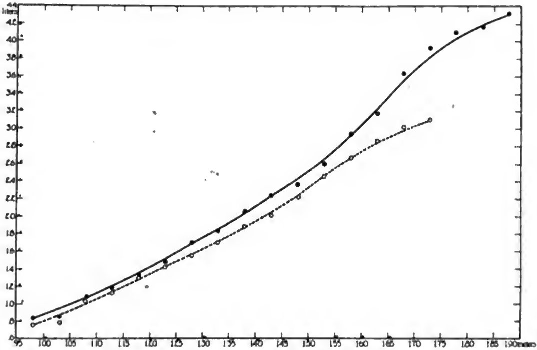

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Fig. 2.—Showing smoothed curves representing the average absolute increase in the vital capacity of the lungs as determined by graphic interpolation, for boys between 0.98 and 1.88 meters tall inclusive, and for girls between 0.98 and 1.73 meters tall inclusive. The actual observed averages at each standing height are represented by dots for boys, and by circles for the girls. Vital capacity in liters is represented on the ordinate, and standing height in meters on the abscissa.

The relative increase in vital capacity accompanying each 5 cm. growth in standing height (Tables 3 and 4) apparently diminishes throughout childhood. There is a slight indication of an increase in percentage growth in vital capacity for the boys between 153 and 168 cm. standing height, and for the girls from 148 to 153 cm. tall. The slight tendency to acceleration in rate after an earlier period of decline is much less striking in the case of the averages based on standing height, as compared with that based on age.

As in the case of the curves for vital capacity as plotted against age, likewise those plotted against standing height may be divided into several phases so selected that each phase conforms very closely to a straight line. The empirical formula $y = (ax) \pm b$ by which each of these straight lines may be derived, therefore, affords a fairly satisfactory method by which the vital capacity at any height may be computed when y = the vital capacity, a = the standing height in cm., x = a constant, and $\pm b$ = a second constant. The vital capacities, as computed by means of the above formula, are recorded in Tables 3 and 4, and, in general, agree fairly closely with the averages as determined by means of graphic interpolation. The constants used in computing the values for each portion of the two curves may be obtained by referring to Tables 3 and 4.

The probable error of random sampling (Tables 3 and 4) computed for the vital capacities as averaged according to standing height, in general, with each sex tends to become larger as the individuals grow taller and have a greater lung capacity. For all groups, however, the probable error is comparatively small.

The standard deviations about the means based on standing height (Tables 3 and 4) for each sex tend to increase as the groups become taller, and are, as a rule, greater for the boys than for the girls of corresponding height. In general, the absolute values obtained for the standard deviation seem to be somewhat greater when the data are averaged in groups differing one year in age, as compared with the deviation occurring when the subjects are averaged in groups differing 5 cm. in standing height.

On reducing the standard deviation to the coefficient of variation (Tables 3 and 4) one finds the vital capacity from each sex to become relatively less variable with increasing height until they become 133 cm. tall. Subsequently the variability increases 2 per cent. for a short period and later declines. The general trend of relative variability in vital capacity with relation to average based upon either age or height are quite similar, in both instances showing a tendency to decrease at first, followed by a period of increased variability, which later declines again. The actual values for the coefficients of variation (Tables 3 and 4), for the most part, vary between 10.5 and 12.5. It appears, therefore, that individual records of vital capacity fluctuating between 12 per cent. above, or 12 per cent. below the average expected for corresponding height, could not be interpreted as definitely abnormal. Should the record vary more than 12 per cent. below the averages, the individual record immediately falls into the class that are apt to be abnormal, and such persons, no doubt, should be examined with care to determine the cause of their low standard of physicla fitness in this respect.

If the coefficients of variation for the averages based on age are compared with those derived from averages based on height, the values will be found to be considerably higher in the former case. Due to the presence of less variability, it appears, therefore, that averages based on grouping of the subjects differing 5 cm. in standing height, for more satisfactory normal standards, than the averages based on age at yearly intervals.

By distributing and averaging the cases at each age according to height, as accomplished in Tables 5 and 6, one is able to gain some conception of the influence of these two factors on the vital capacity. When arranged in this manner it is plainly evident that at any age the taller subjects tend to have a much larger vital capacity than the shorter ones of the same age. This holds true for the girls as well as for the boys. The difference is quite considerable in many instances. Thus, for example, at 14 years of age the average vital capacity for twenty-five girls approximately 150 cm. tall was 2,292 c.c., whereas for thirty-five girls of the same age but approximately 15 cm. taller, the vital capacity averaged 2,824 c.c. or 532 more than for the shorter group. The condition of other ages is similar. It is evident, therefore, that at any age differences in standing height influence the vital capacity to a considerable degree. If we now consider the influence of age on the vital capacity for individuals of about the same standing height no such striking difference is found. In several instances the average vital capacity is slightly greater for the older than for the younger individuals of corresponding average height, but this is not consistently the case. On the whole, it seems clear that the difference in the vital capacity of the lungs among children of the same age but differing considerably in height, is far more striking than the differences noted among children of the same height but of different age. However, in comparing individual records with normal standards it is probably advisable to take both age and height into consideration.

4. *Vital Capacity and Sitting Height.*—In Tables 7 and 8 the data for each sex have been averaged in groups, each group including subjects differing 2 cm. or less in sitting height.

For the boys the averages (Table 7) indicate that with an increase in stem length from 57 to 87 cm. the vital capacity increases from 1,071 to 3,607 c.c. Hence, with a growth of 30 cm. in stem length, the vital capacity shows an average increase of 2,536 c.c., or nearly 237 per cent.

With the girls (Table 8) for a similar growth in sitting height, the vital capacity increases from an average of 908 c.c. at 57 cm. stem length to 2,967 c.c. at 87 cm. stem length. The percentage increase in this case amounts to 197 per cent., or approximately 40 per cent. less than the increase registered by the boys for a similar growth in

TABLE 5.—VITAL CAPACITY, IN CUBIC CENTIMETERS, OF NORMAL BOYS, FOR EACH 5 CM. DIFFERENCE IN STANDING HEIGHT AT EACH AGE, AND AVERAGE VITAL CAPACITY FOR EACH 5 CM. OF GROWTH IN HEIGHT, COMBINING ALL AGES

Age in Years	Standing Height																		
	98	103	108	113	118	123	128	133	138	143	148	153	158	163	168	173	178	183	188
5	837	767	978	975	925	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
6	.....	808	1,122	1,150	1,245	1,333	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
7	.....	.....	1,079	1,215	1,303	1,396	1,620	.....	2,200	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
8	.....	.....	.....	1,242	1,355	1,480	1,707	1,670	1,800	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
9	.....	.....	.....	1,400	1,450	1,537	1,672	1,794	1,992	2,075	.....	.....	.....	.....	.....	.....	.....	.....	.....
10	.....	.....	.....	.....	1,525	1,660	1,662	1,872	2,001	2,227	1,900	.....	.....	.....	.....	.....	.....	.....	.....
11	.....	.....	.....	.....	.....	1,468	1,808	1,827	2,065	2,150	2,184	.....	.....	.....	.....	.....	.....	.....	.....
12	.....	.....	.....	.....	.....	1,300	1,575	1,800	2,059	2,151	2,323	2,655	2,975	3,000	.....	.....	.....	.....	.....
13	.....	.....	.....	.....	.....	.....	.....	1,908	2,132	2,244	2,378	2,546	2,768	3,281	3,400	.....	.....	.....	.....
14	.....	.....	.....	.....	.....	.....	.....	.....	1,938	2,298	2,400	2,584	2,906	3,022	3,328	3,538	3,950	.....	.....
15	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,445	2,565	2,727	2,971	3,200	3,673	3,893	3,862	.....	.....
16	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,400	2,400	2,400	3,236	3,205	3,644	3,958	4,180	.....	.....
17	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,838	2,850	3,813	3,978	4,262	4,050	4,300
18	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,750	.....	3,925	4,125	4,200	4,400	.....
19	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	4,300	4,300	4,300	.....	.....	.....
Absolute increased vital capacity	837	788	1,074	1,190	1,332	1,474	1,690	1,828	2,050	2,230	2,359	2,594	2,936	3,173	3,625	3,919	4,094	4,167	4,300

TABLE 6.—VITAL CAPACITY, IN CUBIC CENTIMETERS, OF GIRLS, FOR EACH 5 CM. DIFFERENCE IN STANDING HEIGHT AT EACH AGE, AND AVERAGE VITAL CAPACITY FOR EACH 5 CM. OF GROWTH IN HEIGHT, COMBINING ALL AGES

Age in Years	Standing Height																	
	88	95	98	103	108	113	118	123	128	133	138	143	148	153	158	163	168	173
4	612	650	692	850	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
5	.....	.....	850	850	914	1,050	1,100	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
6	.....	.....	.....	806	1,034	1,082	1,283	1,317	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
7	.....	.....	.....	950	1,094	1,131	1,239	1,356	1,440	1,800	.....	.....	.....	.....	.....	.....	.....	.....
8	.....	.....	.....	900	1,000	1,231	1,311	1,444	1,455	1,780	.....	.....	.....	.....	.....	.....	.....	.....
9	.....	.....	.....	.....	.....	1,150	1,294	1,430	1,509	1,687	1,820	1,850	.....	.....	.....	.....	.....	.....
10	.....	.....	.....	.....	.....	1,075	1,333	1,423	1,588	1,684	1,821	1,980	2,183	2,150	.....	.....	.....	.....
11	.....	.....	.....	.....	.....	.....	1,325	1,342	1,632	1,703	1,820	1,943	2,143	2,050	.....	.....	.....	.....
12	.....	.....	.....	.....	.....	.....	.....	1,450	1,725	1,700	1,925	1,998	2,110	2,352	2,533	2,950	.....	.....
13	.....	.....	.....	.....	.....	.....	.....	.....	1,650	1,650	1,957	2,020	2,257	2,381	2,515	2,865	3,040	.....
14	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,150	2,200	2,292	2,467	2,678	2,824	3,131	3,100
15	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,210	2,294	2,560	2,708	2,860	3,010	.....
16	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,783	2,786	2,733	2,850	.....
17	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,250	.....	3,030	3,100	.....
Average vital capacity	612	650	756	851	1,022	1,118	1,238	1,412	1,556	1,698	1,870	2,005	2,211	2,449	2,661	2,855	3,017	3,100

TABLE 7.—NORMAL BOYS. NUMBER OF CASES, SITTING HEIGHT, AVERAGE VITAL CAPACITY, VITAL CAPACITY AS DETERMINED BY GRAPHIC INTERPOLATION ABSOLUTE AND PERCENTAGE INCREASE IN VITAL CAPACITY ACCOMPANYING EACH 2 CM. GROWTH IN STEM LENGTH, VITAL CAPACITY AS COMPUTED FROM SITTING HEIGHT BY FORMULA, WITH FORMULA USED IN COMPUTING THE VITAL CAPACITY, CORRECTED SITTING HEIGHT AND VALUES DERIVED FROM FORMULA SQUARE OF SITTING HEIGHT IN CM., PROBABLE ERROR, STANDARD DEVIATION, AND COEFFICIENT OF VARIATION

Number of Cases	Sitting Height, Cm.	Average Vital Capacity, C.c.	Mean Vital Capacity as Determined by Graphic Interpolation, C.c.	Absolute Increase in Vital Capacity with Each 2 Cm. Growth in Standing Height, Cm.	Percentage Yearly Increase in V. C. with Each 2 Cm. Growth in Standing Height, Cm.	Vital Capacity as Computed by Formula $y = (ax) \pm b$	Formula Used for Each Sitting Height Group $y = (ax) \pm b$	Corrected Sitting Height	$\frac{\text{S. H.}^2}{\text{V. C.}}$	Probable Error of Random Sampling, C.c.	Standard Deviation, C.c.	Coefficient of Variation, per Cent.
2	53	975	975	...	...	975	y = V. C.	51.4	2.71	....	...	. . .
7	55	1,036	1,034	59	6.1	1,058	a = Sit. Ht. in Cm.	53.3	2.75	....	...	....
27	57	1,071	1,123	89	8.6	1,141	x = 41.5	55.3	2.72	13.9	151	14.1
51	59	1,190	1,214	91	8.1	1,224	b = —1,224	57.2	2.70	11.3	139	11.7
75	61	1,302	1,307	93	7.7	1,307		59.2	2.68	10.6	187	14.4
78	63	1,425	1,434	127	9.7	1,434	y = V. C.	61.1	2.60	10.9	209	14.7
76	65	1,557	1,576	142	9.9	1,586	a = Sit. Ht. in Cm.	63.1	2.53	12.1	221	14.2
84	67	1,719	1,733	157	10.0	1,738	x = 76	65.0	2.44	12.6	219	12.8
73	69	1,923	1,892	159	9.2	1,890	b = —3,354	66.9	2.42	15.2	217	11.2
78	71	2,054	2,038	146	7.7	2,042		68.9	2.31	15.7	214	10.9
79	73	2,159	2,178	140	6.8	2,194		70.8	2.30	16.4	256	12.0
113	75	2,300	2,326	148	6.8	2,346		72.8	2.28	15.1	239	10.4
85	77	2,497	2,497	171	7.4	2,498		74.7	2.23	18.5	276	11.1
60	79	2,671	2,686	189	7.6	2,686	y = V. C.	76.6	2.18	23.3	287	10.7
91	81	2,881	2,887	201	7.5	2,908	a = Sit. Ht. in Cm.	78.6	2.14	24.5	346	12.0
64	83	3,104	3,104	217	7.5	3,130	x = 111	80.5	2.09	26.2	383	12.3
49	85	3,292	3,342	238	7.7	3,352	b = —6,063	82.5	2.07	31.7	302	12.4
47	87	3,607	3,580	238	7.1	3,574		84.4	1.93	35.5	317	8.8
32	89	3,897	3,796	216	6.0	3,796		86.3	1.96	46.4	328	11.4
16	91	3,913	3,967	171	4.5	3,967	y = V. C.	88.3	1.97			
6	93	4,112	4,123	156	3.9	4,119	a = Sit. Ht. in Cm.	90.2	1.97			
4	95	4,275	4,275	152	3.7	4,273	x = 76.5 b = —2,994	92.2	1.99			

TABLE 8.—NORMAL GIRLS. NUMBER OF CASES, SITTING HEIGHT, AVERAGE VITAL CAPACITY, VITAL CAPACITY AS DETERMINED BY GRAPHIC INTERPOLATION, ABSOLUTE AND PERCENTAGE INCREASE IN VITAL CAPACITY ACCOMPANYING EACH 2 CM. GROWTH IN STEM LENGTH, VITAL CAPACITY AS COMPUTED FROM SITTING HEIGHT BY FORMULA, WITH FORMULA USED IN COMPUTING THE VITAL CAPACITY, CORRECTED SITTING HEIGHT AND VALUES DERIVED FROM FORMULA, SQUARE OF SITTING HEIGHT IN CM., PROBABLE ERROR, STANDARD DEVIATION, AND COEFFICIENT VARIATION

Number of Cases	Sitting Height, Cm.	Average Vital Capacity, C.c.	Mean Vital Capacity as Determined by Graphic Interpolation, C.c.	Absolute Increase in Vital Capacity with Each 2 Cm. Growth in Standing Height, Cm.	Percentage Yearly Increase in V. C. with Each 2 Cm. Growth in Standing Height, Cm.	Vital Capacity as Computed by Formula $y = (ax) \pm b$	Formula Used for Each Sitting Height Group $y = (ax) \pm b$	Corrected Sitting Height	$\frac{S.\ H.^2}{V.\ C.}$	Probable Error of Random Sampling, C.c.	Standard Deviation, C.c.	Coefficient of Variation, per Cent.
1	51	750	750	.....	...	750	(48.6 × Ht.) — 1,728 = V. C.	49.5	3.27			
2	53	1,050	860	+110	14.7	847		51.4	3.08			
10	55	940	956	+ 96	11.2	944		53.3	3.02			
31	57	998	1,038	+ 82	8.6	1,042		55.3	2.95	21.5	177	17.7
48	59	1,107	1,128	+ 90	8.7	1,139		57.2	2.90	12.7	131	11.8
44	61	1,206	1,236	+108	9.6	1,236		59.2	2.84	13.7	159	13.2
71	63	1,386	1,360	+124	10.0	1,360	(65.1 × Ht.) — 2,741 = V. C.	61.1	2.75	10.7	133	9.6
78	65	1,460	1,492	+132	9.7	1,490		63.1	2.67	12.1	159	10.8
69	67	1,636	1,621	+129	8.6	1,620		65.0	2.61	17.3	213	13.0
74	69	1,759	1,747	+126	7.8	1,751		66.9	2.56	16.1	205	11.7
67	71	1,881	1,867	+120	6.9	1,881		68.9	2.54	18.2	221	11.7
57	73	1,952	1,991	+124	6.6	2,011		71.8	2.52	15.6	175	9.0
77	75	2,113	2,124	+133	6.6	2,141		72.8	2.49	17.1	224	10.6
71	77	2,256	2,271	+147	6.9	2,279	(70.5 × Ht.) — 3,149 = V. C.	74.7	2.46	20.5	256	11.3
107	79	2,458	2,420	+149	6.6	2,420		76.6	2.43	20.8	317	12.9
91	81	2,537	2,568	+148	6.1	2,561		78.6	2.41	18.5	261	10.3
80	83	2,740	2,709	+149	5.8	2,702		80.5	2.39	22.1	300	11.3
71	85	2,847	2,843	+134	4.9	2,843		82.5	2.43	22.4	282	9.9
30	87	2,967	2,956	+113	3.9	2,956	(36 × Ht.) + 176 = V. C.	84.4	2.41	44.3	350	12.1
11	89	3,141	3,040	+ 94	3.2	3,028		86.3	2.45			
1	91	3,100	3,100	+ 60	2.0	3,100		88.3	2.51			

sitting height. For both sexes, however, the total relative increase in vital capacity exceeds that for the stem length. Dreyer claims that the vital capacity is related to the square of the sitting height. Whether or not this applies to the period of childhood will be considered later.

The curves of vital capacity as plotted against sitting height are somewhat irregular when drawn from the actual averages. In order to eliminate the minor fluctuations they have been smoothed by means of graphic interpolation (Fig. 3). The means for the vital capacity derived in this manner for each sitting height are recorded in Tables 7 and 8.

In general, the smoothed curves plotted against stem length for each sex are quite similar to those plotted against either age or standing height, showing at first a phase of fairly uniform increase in vital capacity, followed by one of more rapid increase, and finally enters a phase of greater retardation in rate of growth of lung capacity. On the whole, the curves tend to assume a concave form throughout the greater extent of their course, the concavity being more marked with the boys than with the girls. At corresponding sitting height the curves show clearly a greater vital capacity for the boys than for the girls, the difference tending to increase as the growth in stem length occurs.

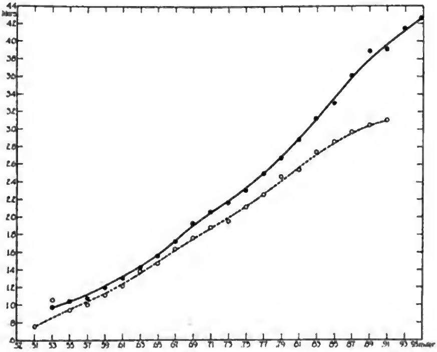

Fig. 3.—Showing smoothed curves representing the average absolute increase in the vital capacity of the lungs as determined by graphic interpolation, for boys with an increase in sitting height from 0.53 to 0.95 meters inclusive and for girls with an increase in sitting height from 0.51 to 0.91 meters inclusive. The actual observed averages at each stem length are respresented by dots for the boys and by circles for the girls. Vital capacity in liters is represented on the ordinate, and sitting height in meters on the abscissa.

The absolute increase in vital capacity which accompanies each 2 cm. increase in sitting height (Tables 7 and 8) is fairly uniform for each sex at stem lengths ranging from 63 to 75 cm. At this point the absolute increase tends to rise reaching a maximum of 238 c.c. for the boys and 149 c.c. for the girls, at stem lengths of 85 and 79 cm., respectively. With each further increase of 2 cm. in sitting height the gain in vital capacity for each sex progressively diminishes.

The relative increase per 2 cm. growth in sitting height, in general, appears to diminish at first as the stem length increases, reaching a minimum of 6.8 and 6.6 per cent. for the boys and girls, respectively, at 73 cm. sitting height. Subsequently, the relative rate of increase in vital capacity rises slightly with the boys to about 7.7 per cent. when the average sitting height is 85 cm., but later declines again. With the girls the tendency for the relative increase in lung capacity to rise after an earlier period of decline is much less pronounced. It appears, however, that the rapidity of the decline in rate of percentage gain in vital capacity is greatly retarded at sitting heights ranging from 73 to 81 cm.

The relation between sitting height and vital capacity has been fully discussed by Dreyer.[20] This investigator states that the relationship between these two measurements may be expressed correctly by the formula $\frac{SH^n}{V.C.} = K$, where SH = stem length in centimeters, V.C. = vital capacity in cubic centimeters, the power n is approximately 2, and K is a constant. In other words, the vital capacity is related to the square of the sitting height. Dreyer bases this opinion on an analysis of the data of Hutchinson and Schuster, on sixteen personal observations, which to a large extent included observations mainly on adults. The average value for the constant obtained by Dreyer when derived in the above manner is 1.9 for males.

Dreyer measured the stem length by a special technic, seating the subject on the floor with his back against a perpendicular triangular projection, to which a scale is attached. On account of the influence of the muscles, the stem length taken when the subject is seated on a chair is found to be about 3 per cent. greater than those obtained by the method Dreyer used. Since the sitting heights for the children reported in this paper were obtained with the subjects seated on a chair, against a perpendicular wall, it is necessary to reduce my averages 3 per cent. to render them directly comparable with the measurements by Dreyer. The corrected sitting heights are recorded in Tables 7 and 8.

The values for K with the boys (Table 7) as derived from the averages of vital capacity for each corrected sitting height during childhood are by no means a constant. The results obtained show a gradual decrease from an average of 2.71 to 1.93 with an increase in sitting height from 53 to 87 cm. With further growth in stem length the value determined for K remains practically constant, possibly tending to increase slightly as sitting height increases. It is evident, therefore, that the formula $\frac{SH^2}{V.C.} = K$ is not a correct expression of the relation between the vital capacity and sitting height for the boys. Apparently this relation is not fully established until well into the latter half of childhood. At this period my data for children give a constant (1.93) which is very close to that obtained by Dreyer (1.90) for adults.

With the girls accompanying a growth in stem length from 51 to 83 cm., the values derived for K decrease from 3.27 to 2.39, but subsequently remains fairly constant.

It is evident, therefore, that a constant relation between the square of the sitting height and vital capacity also does not exist with the girls in early childhood, and apparently is not established until the girls obtain a sitting height of approximately 79 cm.

The higher values for the constant with the girls, indicates a relatively smaller vital capacity of the lungs for them than for the boys.

The probable error of random sampling (Tables 7 and 8), as determined for the averages based on sitting height, is comparatively small. In general, for each sex, it apparently tends to increase constantly as sitting height and vital capacity increases.

The standard deviations recorded in Tables 7 and 8 resemble those obtained when the cases are grouped on different basis, tending to increase as vital capacity increases, and averaging higher, as a rule, with the boys than with the girls of corresponding stem length. As for relative variability (coefficients of variation; Tables 7 and 8) there is an apparent decrease in its extent with the shorter groups as they increase in stem length, followed by a later period where variability rises to some extent, and, finally, by a period during which it falls again. For the most part, the coefficients range between 10 and 14. In general, then, the degree of variability in relation to the averages as based on stem length is quite similar to that observed with averages based on standing height.

If the observations at each age are distributed in groups differing 2 cm. in stem length, as is done in Tables 9 and 10, some conception of the variation in vital capacity at any age accompanying differences in stem length can be easily detected. The averages in these tables show that the vital capacities at every age are higher, as a rule, for the children with the greater stem length. When we consider, however, the average vital capacity for the children of similar sitting height but varying in age the differences are much less striking and constant.

5. *Vital Capacity and Body Weight.*—To study the relation between vital capacity and body weight, the data are averaged in Tables 11 and 12 in such manner that each group included subjects who varied not more than 5 pounds in body weight (including clothing).

TABLE 9.—VITAL CAPACITY, IN CUBIC CENTIMETERS, OF NORMAL BOYS FOR EVERY 2 CM. DIFFERENCE IN SITTING HEIGHT AT EACH AGE, AND AVERAGE VITAL CAPACITY FOR EACH 2 CM. GROWTH IN STEM LENGTH, COMBINING ALL AGES

Age in Years	Sitting Height																					
	53	55	57	59	61	63	65	67	69	71	73	75	77	79	81	83	85	87	89	91	93	95
5	950	800	910	1,025	1,008	1,150	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
6	.....	1,125	1,061	1,172	1,184	1,329	1,200	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
7	1,000	1,150	1,150	1,176	1,300	1,323	1,389	1,460	2,200	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
8	.....	.....	1,200	1,300	1,294	1,424	1,656	1,632	1,825	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
9	.....	.....	.....	1,400	1,517	1,496	1,602	1,764	1,796	1,995	2,500	2,575	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
10	.....	.....	.....	.....	1,525	1,817	1,679	1,728	1,920	1.988	2,031	2,200	2,650	.....	.....	.....	.....	.....	.....	.....	.....	.....
11	.....	.....	.....	.....	.....	1,500	1,767	1,783	1,979	2,088	2,110	2,177	2,500	2,500	.....	.....	.....	.....	.....	.....	.....	.....
12	.....	.....	.....	.....	.....	.....	1,700	1,850	1,950	2,050	2,144	2,241	2,406	2,650	2,788	2,800	.....	.....	.....	.....	.....	.....
13	.....	.....	.....	.....	.....	.....	.....	1,800	2,125	2,060	2,267	2,310	2,423	2,604	2,814	3,012	3,334	.....	4,000	.....	.....	.....
14	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,158	2,100	2,396	2,512	2,650	2,813	3,023	3,221	3,395	3,850	3,450	.....	4,250
15	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,400	2,311	2,688	2,788	2,926	3,269	3,288	3,666	3,853	3,769	.....	.....
16	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,388	2,450	2,675	3,617	3,186	3,373	3,606	3,907	4,125	4.300	4.300
17	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,550	2,900	3,850	4,000	4,167	4,062	4,300
Average	975	1,036	1,071	1,190	1,302	1,425	1,557	1,719	1,923	2,054	2,159	2,300	2,497	2,671	2,881	3.104	3,292	3,607	3,897	3,913	4,142	4,275

TABLE 10.—VITAL CAPACITY, IN CUBIC CENTIMETERS, OF NORMAL GIRLS, FOR EVERY 2 CM. DIFFERENCE IN SITTING AT EACH AGE, AND AVERAGE VTAL CAPACITY FOR EACH 2 CM. GROWTH IN STEM LENGTH, COMBINING ALL AGES

Age in Years	Sitting Height																				
	51	53	55	57	59	61	63	65	67	69	71	73	75	77	79	81	83	85	87	89	91
5	750	950	867	850	1,067	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
6	.....	1,150	983	1,068	1,102	1,100	1,250	1,266	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
7	.....	.....	900	1,094	1,098	1,158	1,353	1,400	1,325	1.400	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
8	.....	.....	.....	1,000	1,192	1,253	1,415	1,474	1,483	1.687	1,750	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
9	.....	.....	.....	.....	1,167	1,383	1,425	1,423	1,540	1,738	1,850	2.000	.....	.....	.....	.....	.....	.....	.....	.....	.....
10	.....	.....	.....	.....	900	1,317	1,404	1,505	1,643	1.749	1,879	2.012	2,175	2,300	2,750	.....	.....	.....	.....	.....	.....
11	.....	.....	.....	.....	.....	1,250	1,431	1,612	1,609	1,773	1,862	1,943	1,975	2,050	2,117	.....	.....	.....	.....	.....	.....
12	.....	.....	.....	.....	.....	.....	1,450	1,450	1,869	1,838	1,867	1,921	2,102	2,258	2,283	2,556	2,700	.....	.....	.....	.....
13	.....	.....	.....	.....	.....	.....	.....	1,700	1,600	1,933	2,000	1,933	2,149	2,236	2,437	2,470	2,713	2,967	2,883	.....	.....
14	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,250	2,230	2.314	2,465	2,596	2,716	2,928	2,958	3,225	.....
15	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,000	2,000	2,150	2,240	2,567	2,686	2,820	2,846	3,029	3,093	.....
16	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,762	2,512	2,550	2,888	3,012	.....	.....
17	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	2,250	2,700	3,017	.....	.....	3,100
18	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	3,100	.....	.....	.....
Average	750	1,050	940	998	1,107	1,205	1,386	1,469	1,636	1,759	1,881	1,952	2,113	2,256	2,458	2,537	2,740	2,847	2,967	3,141	3,100

For the boys (Table 11) with an increase in gross weight from 43 to 133 pounds the vital capacity increased from 1,157 to 3,635 c.c. Accompanying this increase in weight, amounting to 209 per cent., the vital capacity has increased 214 per cent. With the girls (Table 12) for a corresponding growth in weight, the lung capacity increases from 1,099 to 3,047 c.c., or 177 per cent. Thus, while with the boys the relative increase in vital capacity on the average exceeds that in weight, just the reverse is true for the girls.

TABLE 11.—NORMAL BOYS. NUMBER OF CASES, BODY WEIGHT, VITAL CAPACITY, AVERAGE VITAL CAPACITY, AVERAGE VITAL CAPACITY AS DETERMINED BY GRAPHIC INTERPOLATION. ABSOLUTE AND PERCENTAGE INCREASE IN VITAL CAPACITY, VITAL CAPACITY AS COMPUTED BY FORMULA, WITH FORMULA USED, 0.72 POWER OF WEIGHT IN GRAMS AND VALUES DERIVED FROM FORMULA $\frac{W0.72}{V.C.}$

No. of Cases	Gross Wt. in Lbs.	Average Vital Capacity, C.c.	Mean Vital Capacity as Determined by Graphic Interpolation, C.c.	Absolute Increase in Vital Capacity with Each 5 Lbs. Increase in Weight	Percentage Increase, etc., with Each 5 Lbs. Increase in Gross Weight	Vital Capacity as Determined by Empirical Formula $y = ax \pm b$	Empirical Formula $y = (ax) \pm b$	W .72	*$\frac{W\ .72}{V.\ C.}$
2	33	988	988	.....	....	988	y = V.C. in Cm.	942	0.953
13	38	1.135	1.090	+102	11.0	1,098	x = 22.0	1,069	0.958
75	43	1.157	1.198	+108	9.9	1,208	b = +263	1,163	0.955
88	48	1.275	1.319	+121	9.2	1,319	a = Wt. in Lbs.	1,258	0.946
78	53	1,458	1,458	+139	10.5	1,458	y = V.C.	1,343	0.921
82	58	1.607	1.611	+153	10.5	1.598	a = Wt. in Lbs.	1,433	0.896
79	63	1.780	1.765	+154	9.6	1,739	x = 28.1	1,526	0.866
97	68	1.926	1.910	+155	8.8	1,879	b = +30	1,606	0.857
86	73	2,062	2.046	+136	7.1	2,020		1,681	0.833
74	78	2.160	2.178	+132	6.5	2.160		1,764	0.812
96	83	2.284	2,311	+133	6.1	2,301		1,850	0.804
60	88	2,506	2,443	+132	5.7	2,441		1,931	0.790
51	93	2,542	2,574	+131	5.4	2,574	y = V.C. in C.c.	2,014	0.783
45	98	2,687	2,704	+130	5.1	2,710	a = Wt. in Lbs.	2,091	0.772
63	103	2.867	2,841	+137	5.1	2,845	x = 27.2	2,171	0.763
41	108	2,922	2,967	+146	5.1	2,982	b = +44	2,247	0.754
38	113	3,176	3,142	+155	5.2	3,118		2,332	0.740
36	118	3,318	3,297	+155	4.9	3,254		2,410	0.733
32	125	3.397	3,443	+146	4.4	3,443		2,493	0.724
27	128	3,696	3,565	+122	3.5	3,565	y = V.C. in C.c.	2,503	0.721
17	133	3,635	3,680	+115	3.2	3.690	a = Wt. in Lbs.	2,629	0.714
27	138	3,745	3,794	+114	3.1	3,816	x = 25.1	2,710	0.713
13	143	3,815	3,929	+135	3.3	3,941	b = +343	2,795	0.709
9	148	4,217	4,057	+128	3.3	4,067		2,861	0.704
8	153	4.181	4,181	+110	2.7	4,183		2,932	0.701

* W = 0.72 power of the net weight in grams.

The straightened curves derived for vital capacity when averaged for weight are somewhat different in character than those previously described. With the boys the smoothed curve (Fig. 4) shows much less sinuosity than the curves plotted either against age, standing and sitting height. As for the girls the curve based on weight is definitely convex in character, and thus altogether different from those derived from averages determined on the other measurements. The convexity apparently due to the increase in vital capacity occurring at a relatively slower rate than increase in weight during later childhood. As in the case of the curves based on age, standing and sitting height, likewise those plotted against weight may be subdivided into different portions in such manner that each conforms closely to a straight line. It follows, therefore, that the vital capacity may be computed from the body weight by means of the same empirical formula used for the other curves.

TABLE 12.—NORMAL GIRLS. NUMBER OF CASES, BODY WEIGHT, VITAL CAPACITY, AVERAGE VITAL CAPACITY, AVERAGE VITAL CAPACITY AS DETERMINED BY GRAPHIC INTERPOLATION. ABSOLUTE AND PERCENTAGE INCREASE IN VITAL CAPACITY, VITAL CAPACITY AS COMPUTED BY FORMULA, WITH FORMULA USED, 0.72 POWER OF WEIGHT IN GRAMS AND VALUES DERIVED FROM FORMULA $\frac{W^{0.72}}{V.C.}$

No. of Cases	Gross Wt. in Lbs. Including Clothing	Average Vital Capacity, C.c.	Average Vital Capacity as Determined by Graphic Interpolation, C.c.	Absolute Increase in Vital Capacity with Increase in Weight	Percentage of Increase in Vital Capacity with Increase in Weight	Vital Capacity as Computed from Formula y = (ax) ± b	Formula y = (ax) ± b	W 0.72	*W .72 / V. C.
30	38	930	930	.....	....	930	y = V. C.	1,069	1.149
54	43	1,009	1,066	+156	16.8	1,075	a = Wt. in Lbs.	1,163	1.089
63	48	1,244	1,237	+151	13.9	1,220	x = 29	1,263	1.042
86	53	1,388	1,382	+145	11.7	1,365	b = −172	1,356	0.909
76	58	1,527	1,521	+135	9.8	1,510		1,446	0.963
74	63	1,651	1,656	+132	8.7	1,655		1,570	0.948
63	68	1,798	1,786	+129	7.8	1,788	y = V. C.	1,624	0.914
78	73	1,918	1,917	+129	7.2	1,908	a = Wt. in Lbs.	1,713	0.900
60	78	2,029	2,046	+124	6.5	2,028	x = 24	1,800	0.887
61	83	2,207	2,170	+122	6.0	2,148	b = +156	1,885	0.879
69	88	2,271	2,292	+114	5.2	2,268		1,967	0.878
64	93	2,428	2,406	+103	4.5	2,388		2,047	0.860
64	98	2,520	2,509	+ 84	3.5	2,508		2,132	0.850
57	103	2,620	2,593	+ 67	2.7	2,593	y = V. C.	2,208	0.851
48	108	2,720	2,660	+ 68	2.6	2,660	a = Wt. in Lbs.	2,291	0.862
36	113	2,628	2,728	+ 77	2.8	2,727	x = 13.4	2,361	0.867
32	118	2,803	2,805	+ 80	3.3	2,794	b = +1,213	2,527	0.882
28	123	2,900	2,894	+ 78	2.8	2,861		2,569	0.884
15	128	3,037	2,972	+ 55	1.9	2,928		2,663	0.889
15	133	3,047	3,027	+ 34	1.1	2,995		2,743	0.896
14	138	3,061	3,061	+ 34	1.1	3,062			
6	143	2,725							
4	148	3,000							
4	158	3,388							
2	173	2,900							
28	123	2,900	2,894	+ 78	2.8	2,861		2,569	0.884
1	193	2,900							

* W = 0.72 power of the net weight in grams.

The actual values for the constants to be used for different weight groups may be determined by referring to Tables 11 and 12. The vital capacities computed from formula agree fairly closely with the actual averages and also with those as determined by graphic interpolation.

Dreyer[20] claims that the relation between the vital capacity and body weight may be correctly expressed by the formula $\frac{W^n}{V.C.} = K$, where

W is the net weight in grams, V.C. = vital capacity in cubic centimeters, the power n is 0.72, and K = a constant. The average value obtained for K by Dreyer for data collected largely from male adults is 0.69.

In order to compare this relationship to body weight for children with Dreyer's findings for adults it was first necessary to correct my weights for clothing. The net weight for my cases has been determined by computing the weight of the clothing and deducting this from the gross weight. In estimating the weight of clothing the factors published by Bardeen [5] were used and the net weights obtained in this manner are tabulated in Tables 11 and 12.

With the boys the values obtained for K by means of the formula $\frac{W^{72}}{\text{V.C.}} = K$ are seen to decrease constantly as growth in body weight occurs, diminishing from an average of 0.955 at a net weight of 40 pounds (18,100 gm.) to 0.701 when weighing 143.8 pounds (65,400 gm.). This latter value, 0.701, is quite similar to that (0.69) obtained by Dreyer for adults. It is evident from these results that the constant relation between the 0.72 power of the weight and vital capacity is not established with boys until the net body weight is in the neighborhood of 140 pounds.

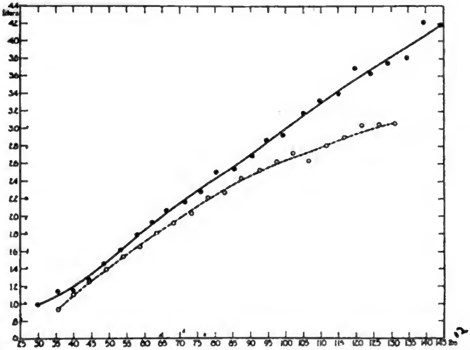

Fig. 4.—Showing smoothed curves representing the average absolute increase in the vital capacity of the lungs as determined by graphic interpolation for boys with an increase in net body weight from 30 to 145 pounds inclusive, and for girls with an increase in body weight from 35 to 130 pounds inclusive. The actual observed averages at each net body weight are represented by dots for the boys, and by circles for the girls. Vital capacity in liters is represented on the ordinate, and net weight in pounds on the abscissa.

With the girls the value for K with an increase in net weight from 40 to 92 pounds decreases from 1.089 to 0.850. With further increase in weight the value for K seems to increase slightly. For the girls also, then, the formula advocated by Dreyer is not a correct expression of the relation of vital capacity to body weight for children. It is not until the latter part of childhood that the above relation is fully established. At corresponding age, the values obtained for K (Tables 11 and 12) are higher for the girls than for the boys. It follows from this, as shown in numerous other instances, that lung capacity is relatively smaller for girls than for boys of similar size

TABLE 13.—Number of Cases, Age, Weight, Standing Height, Vital Capacity, Normal Vital Capacity Expected for Corresponding Standing Height, Per Cent. of Deviation from Normal, and Note Regarding Dyspnea for Boys and Girls with Mitral Regurgitation

Average No. of Cases	Average Age, Years	Average Net Weight, Lbs.	Average Standing Height, Cm.	Average Vital Capacity, C.c.	Average Normal Vital Capacity for Corresponding Height, C.c.	Average per Cent. of Deviation from Normal	Notes Regarding Dyspnea
Boys 8	11	74.6	142	2,131	2,182	— 2.4	No dyspnea on exertion
Girls 17	12	77.4	144	1,939	2,006	— 3.2	No dyspnea on exertion
Boys							
1	7	40	112	900	1.100	—22.4	Spleen enlarged; moderate dyspnea; râles in lungs
2	15	57	131	775	1,780	—56.5	Dyspnea pronounced
3	11	55	133	1,600	1.850	—13.5	Dyspnea on mild exertion
4	15	61	148	1,300	2,230	—41.7	Dyspnea on slight exertion
5	16	102	162	1,350	3,180	—57.5	Dyspnoic constantly
6	18	122	174	2,100	3,860	—45.6	Dyspnea on slight exertion
Girls							
1	9	40	121	950	1,360	—30.1	Dyspnoic
2	11	62	129	1,100	1,580	—30.4	Slight dyspnea
3	12	52	127	900	1,525	—41.0	Mild dyspnea on exertion
4	11	62	129	1,100	1,590	—30.8	Moderate dyspnea
5	13	87	145	900	2,110	—57.3	Severe dyspnea
6	13	80	146	1,250	2,150	—41.9	Moderate dyspnea
7	20	117	150	1,500	2,310	—35.1	Moderate dyspnea
8	14	83	152	1,200	2.400	—50.0	Dyspnea on slight exertion
9	16	120	163	1,950	2,830	—31.0	Considerable dyspnea

Although the present investigation is devoted mainly to a consideration of the vital capacity of the lungs of normal and healthy children, a series of observations were made on a considerable number of subjects suffering from pathologic conditions of the heart and lungs. A brief discussion of the results obtained in each disease is given below.

6. *Vital Capacity and Mitral Insufficiency.*—Records were obtained for fourteen boys and twenty-six girls suffering from mitral insufficiency of varying degrees of severity (Table 13). The data for eight boys and seventeen girls show the vital capacity to average practically normal for their standing height in spite of the presence of a

leaking mitral valve. These children, as a group, are able to play and romp almost as vigorously as normal children without suffering from dyspnea to any extent. With the more severe cases, however, the vital capacity is seen to be greatly reduced, the reduction in some cases amounting to more than 50 per cent., and in such instances dyspnea is a very prominent symptom. In general, it may be said, that the tendency to become dyspneic is directly proportional to the degree to which the vital capacity is reduced. Ruebow,[14] Bittorf and Forschbach,[23] Beebak, Bie and Maar,[16] Plesch,[17] Wilson and Edwards,[24] and others have also noted the vital capacity to be reduced by diseases of the heart. Siebeck[15] attributes the decrease in vital capacity in heart disease to a change in the elasticity of the lungs resulting from engorgement of the pulmonary circulation. From a study of 124 adults suffering from various types of heart disease, Peabody and Wentworth[18] have decided that, in general, patients with a vital capacity of 90 per cent. or more of the normal standard adopted for their sex and height have little or no abnormal tendency to dyspnea. If reduced to 70 or 90 per cent. of the normal, dyspnea appears to be an unusual exertion, while if reduced to 40 or 70 per cent. of the normal the activities of these patients must be greatly restricted. Those with a vital capacity of less than 40 per cent. of the normal are usually confined to bed, and the mortality is high with this group.

Repeated observations made of a few children having mitral disease show that the vital capacity increases as the clinical condition improves. The record for one girl with mitral regurgitation and rheumatic fever is given in Figure 5. The record of a girl suffering from cardiac decompensation following a heavy day's work is given in Figure 6. In each instance the vital capacity is seen to progressively increase, and the hospital records show a similar improvement in their condition clinically. With the older girl (Fig. 6) the reduction in vital capacity recorded on the twenty-sixth day of illness followed a tonsillectomy done two days previously. When dismissed from the hospital on the twenty-eighth day of illness the vital capacity recorded was considerably higher even than the normal expected for corresponding standing height.

Peabody and Wentworth and Ulrich and Nathanson[25] also present records for adults that show fluctuations in the vital capacity to correspond with changes in the patient's condition. Periodic measure-

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[23] Bittorf, A., and Forschbach, J.: Untersuchungen über die Lungenfüllung bei Krankheiten, Ztschr. f. klin. Med. **70,** 1910.

[24] Wilson, M. G., and Edwards, D. J.: Standards for Normal Vital Capacity for Children: The Lung Capacity in Certain Intrathoracic Conditions, Am. J. Dis. Child. **22**:443 (Nov.) 1921. Diagnostic Value of Determining Vital Capacity of Lungs of Children, J. A. M. A. **78**:1107 (April 15) 1922.

[25] Ulrich, H. L., and Nathanson, M. H.: The Capacity of the Lungs in Cardiac Disease, Minnesota M. **4**:721, 1921.

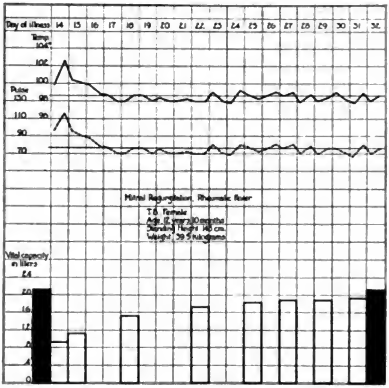

Fig. 5.—Showing the changes in body temperature, pulse rate, and vital capacity of the lungs from the fourteenth to the thirty-first day of illness, for a girl having acute rheumatic fever, and mitral regurgitation. The solid black rectangles represent the normal vital capacity for corresponding standing height; the blank rectangles represent the observed vital capacity on successive days.

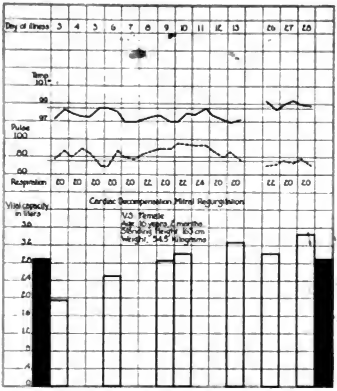

Fig. 6.—Showing the changes in body temperature, pulse rate, rate of respiration and vital capacity of the lungs from the third to the thirteenth and for the twenty-sixth to the twenty-eighth day of illness, for a girls cardiac decompensation, and mitral regurgitation. The solid black rectangles represent the normal vital capacity for corresponding standing height; the blank rectangles represent the observed vital capacity on successive days.

ment of the vital capacity, therefore, affords a simple and practical method of detecting fluctuations in the general condition of the patient.

This study of a limited number of children suffering from disease of the mitral valve shows that in milder cases in which the vital capacity is practically normal very little respiratory discomfort is experienced even on severe exertion. In more severe cases, however, the tendency to develop dyspnea in a measure parallels the reduction in vital capacity.

7. *Vital Capacity and Acute Bronchitis.*—In Table 14 are recorded the average vital capacities for seventeen boys and fourteen girls, respectively, having acute bronchitis, which shows that the vital capacity is considerably reduced by this condition. The individual data show the degree of reduction to be rather marked in the more severe cases. Often the presence of considerable mucus in the trachea and bronchi provokes peroxysms of coughing toward the end of expiration, and thus prevent its completion. Even with the patients showing the greatest reduction in vital capacity due to their bronchitis, there was little complaint of dyspnea. Peabody and Wentworth also record that the vital capacity of the lungs may be considerably reduced following the inception of acute bronchitis.

TABLE 14.—NUMBER OF CASES, AGE, WEIGHT, STANDING HEIGHT, VITAL CAPACITY, NORMAL VITAL CAPACITY FOR CORRESPONDING STANDING HEIGHT, AND PER CENT. OF DEVIATION FROM NORMAL FOR BOYS AND GIRLS HAVING ACUTE BRONCHITIS

Average Number of Cases	Average Age, Years	Average Gross Weight, Lbs.	Average Standing Height, Cm.	Average Vital Capacity, C.c.	Average Normal Vital Capacity for Corresponding Standing Height	Average Per Cent. Deviation from Normal
Boys..... 17	10	65.3	131	1,450	1,795	—18.9
Girls..... 14	10	68.1	131	1,354	1,650	—17.9

8. *Vital Capacity and Labor Pneumonia.*—During the past year vital capacity records were obtained of eleven children during an attack of pneumonia. The data for nine of the children (Table 15) show the vital capacity to be enormously reduced early in the course of the disease. The degree of reduction is greatly out of proportion to the extent of the pneumonic process even with patients not suffering from pleurisy. For example, one boy (Case 1) on the fifth day of illness, although free from pleurisy, was able to expire only 450 c.c., which is about one third the normal expected for corresponding standing height. At the same time, fluroscopic examination demonstrated the pneumonia to be limited to the lower lobe of the right lung. In this instance, although, roughly, one fourth or less of the total lung tissue was involved by the pneumonic process, nevertheless, the vital capacity

was reduced by three fourths. In other cases the reduction is equally striking. The general weakness of the patient is evidently a factor in reducing the vital capacity.

The initial reduction in vital capacity, and its gradual return to normal following recovery from lobar pneumonia is clearly shown for two boys in Figures 7 and 8. In the case of the older patient (Fig. 7), on the second day of illness the vital capacity was reduced 35 per cent. At this time the clinical diagnosis was somewhat uncertain. On the fourth day, however, a diagnosis of lobar pneumonia was definitely established, and the vital capacity was now reduced approximately 71 per cent. Following the crisis the vital capacity gradually increased and by the seventeenth day of illness was only slightly more than 17 per cent. below the normal expected for corresponding standing height. For this patient a record of vital capacity was obtained nine months following his recovery from pneumonia. During this interval the records show an increase in vital capacity from 2,850 c.c. to 3,500 c.c. This indicates that following recovery from an attack of pneumonia, subsequent growth in lung capacity may proceed in a rather satisfactory manner.

TABLE 15.—Number of Cases, Age, Standing Height, Weight, Initial Vital Capacity, Day of Illness, Vital Capacity at Each Succeeding Reading, Normal Vital Capacity for Corresponding Standing Height, Per Cent. of Deviation from the Normal for Boys and Girls with Lobar Pneumonia

No.	Standing Height, Cm.	Net Weight, Lbs.	Initial Vital Capacity and Day of Illness	Vital Capacity at Each Succeeding Reading						Normal Vital Capacity for Corresponding Standing Height	Per Cent. of Deviation from the Normal
Boys											
1	118	50	4 350	5 450	6* 800	9 1,050	12 1,250	.....	.....	1,340	— 6.7
2	116	51	6 750	8* 1,000	14 1,225	.....	.....	.....	.....	1,280	— 4.3
3	134	65	3 4 400	4 7* 600	5 8 700	7* 9 900	8 14 750	9 50 800	10 71 1,200	1,880	—36.2
4	135	59	3 850	13 1,350	20 1,600	25 1,700	.....	.....	.....	1,920	—11.5
Girls											
5	106	39	1 150	6 750	7* 775	10 800	12 850	.....	.....	950	—10.6
6	123	...	7* 700	9 750	12 800	14 900	15 1,000	16 1,100	.....	1,410	—22.0
7	43	...	4 350	6* 1,000	8 1,100	10 1,250	.....	.....	.....	2,030	—38.4
8	133	62	10 800	12 900	15 1,300	19 1,550	.....	.....	.....	1,510	+ 2.6
9	155	960	6 300	9 675	12 1,000	16 1,500	20 1,650	23 2,000	26 2,050	2,520	—18.7

* Day of crisis.

One child (Case 3) failed to recover promptly. Areas of consolidation persisted in one lung for a long time which, finally, terminated in an empyema. The records show that during the period studied the

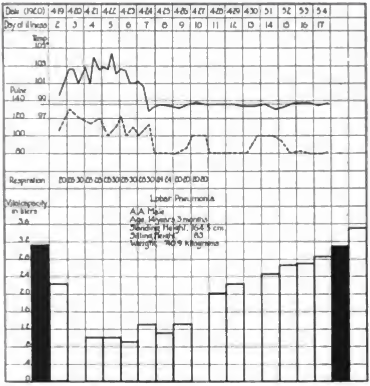

Fig. 7.—Showing the changes in body temperature, pulse rate, rate of respiration and the vital capacity of the lungs from the second to the seventeenth days of illness, for a boy having lobar pneumonia. The solid black rectangles represent the normal vital capacity for corresponding standing height; the blank rectangles represent the observed vital capacity on successive days.

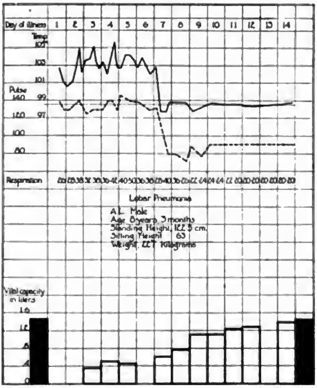

Fig. 8.—Showing the changes in body temperature, pulse rate, rate of respiration, and the vital capacity of the lungs from the first to the fourteenth day of illness, for a body having lobar pneumonia. The solid black rectangles represent the normal vital capacity for corresponding standing height; the blank rectangles represent the observed vital capacity on successive day.

vital capacity remained considerably below normal. Accompanying slight improvements in the patient's general condition, the vital capacity increased slightly, but decreased again when he felt worse. At the time the last observation was made the vital capacity was still 36 per cent. below the expected normal.

During the course of this investigation the disappearance of physical signs was observed in several instances to precede the complete return of vital capacity to normal.

9. *Vital Capacity and Bronchial Asthma.*—Several patients subject to attacks of asthma visited the dispensary during the past winter. The vital capacity records for these children are tabulated in Table 16. The data show that the vital capacity, even with children who have experienced severe asthmatic attacks for several years, may be practically normal during intervals when they are free from symptoms. However, immediately following acute attacks, when the lungs show marked evidence of the disease, the vital capacity may be reduced greatly (Cases 1, 2, 7 and 14). The greatest reduction noted in this study amounted to 47.7 per cent. in Case 7. For one patient (Case 2) the vital capacity was recorded during an acute attack, and also again at a later time when he was free from symptoms. In this instance,

TABLE 16.—NUMBER OF CASES, AGE, WEIGHT, STANDING HEIGHT, VITAL CAPACITY, NORMAL VITAL CAPACITY FOR CORRESPONDING STANDING HEIGHT, PER CENT. OF DEVIATION FROM NORMAL AND CLINICAL NOTES FOR BOYS AND GIRLS SUBJECT TO BRONCHIAL ASTHMA

No. of Cases	Age, Years	Gross Weight, Lbs.	Standing Height, Cm.	Vital Capacity, C.c.	Normal Vital Capacity for Corresponding Standing Height	Per Cent. of Deviation from Normal	Clinical Notes: Duration of Disease
Boys							
1	6	32	109	750	1,080	—30.6	Many râles present
2	6	39	113	775	1,190	—34.9	Many râles present
3	6	45	118	1,600	1,340	+19.4	No râles present
4	6	41	118	1,550	1,340	+15.7	No râles present
5	8	48	123	1,900	1,500	+26.7	No râles present; asthma for 6 years
6	7	48	123	1,450	1,500	— 3.3	Few râles present; asthma for 4 years
7	8	57	124	800	1,530	—47.7	Many râles present
8	10	64	132	1,900	1,810	+ 5.0	Asthma for 3 years; no râles present
9	11	64	132	1,800	1,810	— 0.5	
10	12	63	140	2,350	2,100	+11.9	Few râles present; asthma for 4 years
11	13	63	145	2,350	2,300	+ 2.2	Asthma for 9 years
12	11	72	146	1,950	2,340	—16.7	Asthma for 2 years; no râles present
13	14	104	155	3,200	2,760	+15.9	Eight years
Girls							
1	7	38	119	900	1,300	—30.8	Many râles present; 3 years
2	9	46	120	1,275	1,330	— 4.1	No râles present
3	9	50	130	1,800	1,620	+11.1	Few râles present
4	13	65	...	2,500	.....	......	No râles present; 7 years

during the attack, his vital capacity was nearly 35 per cent. below normal, whereas after the symptoms disappeared it actually exceeded the normal expected for his standing height almost 12 per cent.

From this study of a limited number of cases the conclusion seems justified that while bronchial asthma may cause an enormous reduction in the vital capacity immediately following an acute attack, nevertheless, the reduction promptly disappears and the vital capacity returns to normal as the symptoms subside. Even in cases subject to the disease for several years there is apparently no permanent reduction in vital capacity.

Peabody and Wentworth note that with adults the vital capacity becomes greatly lowered during asthmatic attacks. Four patients tested soon after acute attacks were found to have vital capacities of 56, 60, 85 and 102 per cent. of the normal, respectively. Seven observations on six patients made when they were in their best condition between asthmatic spells showed a range in vital capacity between 65 and 122 per cent. of the normal. In only one case was it below 85 per cent.

TABLE 17.—Age, Number of Cases, Net Weight, Standing Height, Vital Capacity, Normal Vital Capacity for Corresponding Standing Height, and Per Cent. That Observed Vital Capacity Deviated from the Normal, for Children of Fresh Air School

Average Age, Years	Average Number of Cases	Average Weight, Kg.	Average Standing Height, Cm.	Average Vital Capacity, C.c.	Average Normal Vital Capacity for Corresponding Standing Height, C.c.	Average per Cent. Deviation from Normal
Boys..... 11	46	33.0	142.8	2,055	2,182	—5.8
Girls..... 11	51	32.8	140.0	1,842	1,925	—4.3

10. *Vital Capacity and Tuberculosis.*—In Table 17 are recorded the vital capacities of forty-six boys and fifty-one girls, all of whom were attending what is known as the fresh air school. Children are eligible for admission to this school only in case they have a positive Pirquet (tuberculin) reaction, and show some clinical evidence of tuberculosis, such as slight daily elevation in temperature, frequent attacks of bronchitis or failure to gain in weight properly. Physical examination of the lungs in most instances was practically negative, except for the usual presence of a positive D'Espine sign, and, as a rule, the roentgen-ray findings were limited to enlarged peribronchial lymph glands at the hilus of the lungs. The condition of this group of cases is probably fairly representative of the usual early type of quiescent tuberculosis encountered in children.

The vital capacity of the lungs for the boys (Table 17), while tending to be slightly low in many cases, in general, agrees fairly well with normal averages for corresponding height. The reading for only five of the boys appeared to be definitely subnormal. However, on comparing the stem length of each of these boys with the normal as found by Boas [26] for corresponding height, in each instance the observed sitting height is found to be considerably less than that expected of boys of their height. Since standing height seemed rather abnormal with these boys as compared with their sitting height, it was thought that the records would probably agree more closely with averages of vital capacity based on stem length. When the observed vital capacities was compared with the normal expected for corresponding stem length in each instance, the vital capacity appears to be practically normal as compared with the normal for corresponding sitting height. In general, then, it is doubtful if the lung capacity of any of these forty-six boys can be considered as definitely abnormal in this respect.

For the girls (Table 17) the average vital capacity agrees fairly well with the normal expected for corresponding standing height. In only four instances were the readings significantly subnormal.

While the number of observations is too small to permit of very sweeping conclusions, nevertheless, the data indicate that the vital capacity is usually normal in children reacting positively to the intracutaneous application of old tuberculin and showing little additional evidence of tuberculosis aside from a positive D'Espine and a comparatively poor health record. Certain of these children, however, have an abnormally low vital capacity. These may be the ones who are most likely to develop serious forms of the disease in the future. Later determinations of their vital capacity, if showing a further decrease, would probably give immediate clue to any change in their pulmonary condition.

In addition to these children showing a minimum evidence of tuberculosis, the lung capacity also of twenty-six boys and seventeen girls with definite tuberculosis of bone was studied. The data obtained from this series of patients are recorded in Table 18. The average value for the readings for each sex appear to be practically normal for standing height. For a few of the individuals, however, the lung capacity was abnormally low, especially with the more serious cases. For one boy the reduction amounted to 40 per cent. This boy has a marked kyphosis of the midthoracic region which is completely ankylosed. The marked deformity and resultant mechanical interference with inspiration probably accounts partly for his low vital capacity, especially since the lungs are apparently normal.

For another patient the vital capacity was 46.4 per cent. below the normal expected. This patient was in a very poor general condition,

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26. Boas, F., and Wissler, C.: Statistics of Growth, U. S. Education Commision **1,** 1904.

weighing only 49 pounds, and has an active tuberculosis of the lower lumbar spine with a psoas abscess and several discharging sinuses. The roentgen ray also revealed a marked shadow about the hilus and considerable mottling throughout the lung field. Six months later the vital capacity was recorded a second time and during this period was found to have decreased from 1,050 c.c. to 750 c.c., a decrease of about 29 per cent. At this time his condition was definitely worse than at the previous examination. In this instance one, no doubt, would suspect the above to be true merely from considering the vital capacity record alone, even without knowing other facts about the case.

TABLE 18.—NUMBER OF CASES, AGE, WEIGHT, STANDING HEIGHT, VITAL CAPACITY, NORMAL VITAL CAPACITY FOR CORRESPONDING STANDING HEIGHT, LOCATION AND EXTENT OF DISEASE FOR BOYS HAVING TUBERCULOSIS OF BONE AND LUNGS

Number of Cases	Average Age, Years	Average Net Weight, Lbs.	Average Standing Height, Cm.	Average Vital Capacity, C.c.	Average Normal Vital Capacity for Corre-Standing Height	Average per Cent. of Deviation from Normal	Average Location and Extent of Tuberculosis
Girls 17	10	50.5	125	1,401	1,470	— 4.9	Tuberculosis of hip, knee, spine, etc.
Pulmonary Tuberculosis							
1	13	55	135	575	1,770	—67.5	Advanced pulmonary; extensive cavity formation
2	16	82	157	1,000	2,610	—61.7	Advanced pulmonary; extensive cavity formation
3	18	110	151	1,000	2,350	—57.4	Advanced pulmonary; extensive cavity formation
Boys 26	11	59.5	128	1,542	1,700	— 9.3	Tuberculosis of hip, knee, spine, etc.
Pulmonary Tuberculosis							
1	9	61	123	1,000	1,490	—32.9	Lungs, with effusion (incipient)
2	11	85	145	2,250	2,300	— 2.2	Lungs (incipient)
3	12	60	145	1,000	2,300	—56.5	Lungs (chronic fibroid), peritoneum
4	15	107	177	2,900	3,980	—27.1	Lungs (moderately advanced)
5	16	108	157	2,700	2,880	— 6.2	Lungs (incipient)
6	18	50	*	750	4,300*	—82.6	Spine, lungs
7	17	81	157	1,100	2,880	—61.8	Lungs (advanced), spine

* V. C. for corresponding age.

For the seventeen girls (Table 18) having tuberculosis of the bone the average for the vital capacity is practically normal. The volumes for two subjects of this group, however, were abnormally low, being 25.6 and 35.5 per cent., respectively, below the normal for corresponding height. With these two girls observations six months later show in each instance an increase of about 100 c.c., in vital capacity. The gain in lung capacity registered by these patients during this period probably indicates a better prognosis than in the case mentioned above in which the vital capacity decreased to a considerable extent.

In only a few instances was it possible to obtain observations of the vital capacity of the lungs of children with definite and active pulmonary tuberculosis. Data for ten such cases are recorded in Table 18. Of the incipient cases only one boy (Case 1) has a vital capacity significantly subnormal. In this instance the presence of a pleural effusion probably accounts for a considerable portion of this reduction. In Case 2 the lung capacity is practically normal. The roentgenogram of this patient's lungs revealed a rather large shadow extending from the hilus out into the parenchyma of the right lung; and the Pirquet reaction was strongly positive. About one months after the vital capacity was recorded for the first time, this boy had a tonsillectomy following which he developed a tuberculous meningitis and promptly died. This case illustrates, therefore, that a normal vital capacity may be obtained even in the presence of a pathological pulmonary condition of the most serious potentialities.

Among the advanced cases, two patients (Cases 3 and 9) have died during the past few months. In these cases, however, death was not unexpected for in both the tuberculous process was very extensive. It is interesting to note that of the advanced cases four patients (Cases 6, 7, 8 and 9) were ambulatory and suffered no dyspnea on mild exertion in spite of the fact that their vital capacities were reduced to about one third their normal value. This observation stands out in marked contrast to these symptoms noted in cardiac disease for with a similar reduction in vital capacity dependent on some pathologic condition of the heart, dyspnea is a constant and very prominent symptom.

Many investigators, including Hutchinson, Wintrich, Scheevoogt, Arnold, Fabius, Schönfeld,[27] Siebeck, Wilson and Edwards, and others, have observed that the vital capacity may be reduced greatly in the presence of pulmonary tuberculosis. Recently Dreyer and Burrell[20] have been able to classify cases of pulmonary tuberculosis as normal or as incipient, moderate or advanced, without seeing the patients, knowing only their vital capacity and various body measurements.

From a study of patients with incipient tuberculosis Garvin, Lundsgaard and Van Slyke[28] found the vital capacity to be reduced as a result of an increased residual air. In moderately advanced and advanced cases the vital capacity was substantially reduced principally as a result of diminished total lung capacity. The residual air was normal, as a rule, although in a few cases an increase in residual air also contributed to the decrease in vital capacity.

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[27] Schonfeld, L.: Ein Beitrag zur Lehre von der Spirometrie, Diss. Berlin 1882.

[28] Garvin, A.; Lundsgaard, C.; Van Slyke, D. D.: Studies of Lung Volume II Tuberculous Men, J. Exper. M. **27**:87, 1918. Studies of Lung Volume III, Tuberculos Women, J. Exper. M. **27**:129, 1918.

Wittich, Meyers and Jennings [29] found the vital capacity to decrease relative to body weight, in direct proportion to the amount of disease present.

CONCLUSIONS

From this study it appears evident that the determination of the vital capacity of patients having diseases of the heart and lungs is of distinct clinical value. Although single observations are of importance, repeated measurements are of much greater value, for changes in the pathologic condition of these organs is immediately reflected by fluctuations in the vital capacity. It is undoubtedly inadvisable to use the determination of the vital capacity to the exclusion of other means of making a diagnosis, for occasionally this measurement is very misleading, and might easily lead to serious error if relied on alone. However, with the exercise of proper judgment and care, one usually is able to use the information gained through the measurement of the vital capacity safely and profitably in determining not only the presence but also roughly the extent and progress of the disease of the heart and lungs.

SUMMARY

The more important results of the present investigation may be summarized briefly as follows:

1. At either corresponding age, standing height, sitting height, or body weight the vital capacity of the lungs is constantly greater with the boys than with the girls, the difference increasing with the especial rapidity during the latter half of childhood.[30]

2. The curves of vital capacity as plotted against age, standing and sitting height, in general, pursue a sinuous course, showing a fairly uniform increase at first, followed later by a period of more rapid growth in lung capacity, which later diminishes in rate. The curve plotted against body weight for the boys shows a more uniform course, while that for the girls has a definitely convex form.

3. The absolute annual increase in vital capacity, in general, is fairly uniform during early childhood, increases in rapidity about the time of puberty, and later declines.

4. The relative increase in vital capacity apparently decreases at first, becomes relatively more rapid about the time of puberty, and

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[29] Wittich, F. W., Myers, J. A., and Jennings, F. L.: A Study of the Effect of Pulmonary Tuberculosis on Vital Capacity, J. A. M. A. **75**:1249 (Nov. 6) 1920.

[30] Emerson, P. W., and Green, H.: Vital Capacity of the Lungs of Children, Am. J. Dis. Child. **22**:202 (Aug.) 1921.

then proceeds at a slower rate again. The period of acceleration in the rate of growth in lung capacity begins and terminates at an earlier age with the girls than with the boys.

5. Throughout childhood the vital capacity formed a greater proportion of the estimated adult maximum (3,200 c.c.) for women with the girls, than with the boys, the adult maximum of the latter be estimated as approximately 4,300 c.c. In general, then, with respect to lung capacity, at corresponding ages the girls may be considered relatively more mature than the boys.

6. The vital capacity of the lungs apparently reaches a maximum near the twentieth year with the boys, and probably slightly before this time with the girls.

7. On using the proper values for the constant, the vital capacity may be computed[31] fairly accurately from the age, the standing height, the sitting height or the body weight by means of the empirical formula $y = (AX) \pm b$, where $y =$ vital capacity in cubic centimeters; $a =$ (either age in years, standing height or sitting height in cubic centimeters or body weight in pounds), $X =$ a constant, and $\pm b =$ a second constant. The proper values for the constants may be determined by referring to the appropriate tables.

8. The probable error of random sampling increases as the vital capacity increases, but in all instances is relatively small, amounting to less than 25 c.c., as a rule. Therefore, averages obtained from an infinitely large number of comparable series would vary only slightly from those obtained in the present limited series of observations.

9. The standard deviation (absolute variability), as a rule, increases as the vital capacity increases, and usually is greater with the boys than with the girls of corresponding age and size.

10. The coefficient of variation (relative variability) for each sex decreases during early childhood, increases about the period of puberty and later declines again. The extent of the dispersal of the individual observations from the averages, appears to be smaller when averaged in groups differing 5 cm. in standing height or 2 cm. in stem length, than when averaged according to age in years, as estimated from the nearest birth day.

11. The constant relation between the vital capacity and the square of the sitting height, and also between the 0.72 power of the body weight in grams and the vital capacity apparently is not established until the latter part of childhood.

12. Children may have a normal vital capacity even in the presence of a definite insufficiency of the mitral valves, and these individuals show

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[31] West, H. F.: Clinical Studies on the Respiration. VI. A Comparison of Various Standards for the Normal Vital Capacity of the Lungs, Arch. Int. Med. **25**:306 (March) 1920.

little abnormal tendency to dyspnea on exertion. In more serious cases the vital capacity is greatly reduced, and the tendency to respiratory embarrassment is proportional to the reduction in lung capacity.[32]

13. When the condition of the heart improves, the vital capacity gradually increases.

14. Acute bronchitis produces a temporary reduction in vital capacity, which in severe cases may be very marked.

15. During the course of lobar pneumonia the vital capacity rapidly undergoes an enormous reduction, even in cases free from pleurisy. The reduction is altogether out of proportion to the extent of the pneumonic process in the lungs. Following the crisis, the vital capacity gradually returns to normal, in a comparatively short time. Physical signs of the disease, however, may disappear before the normal vital capacity is reached. In complicated cases the return of vital capacity to normal may be greatly delayed.

16. While bronchial asthma may cause an enormous reduction in the vital capacity immediately following an acute attack, nevertheless the reduction promptly disappears as the symptoms subside. Even in children subject to the disease for several years, there is apparently no permanent reduction in the vital capacity of the lungs.

17. With children showing slight evidence of tuberculosis, such as a positive Pirquet (tuberculin) reaction, and having a poor health record, and also with those having definite tuberculosis of bone, the vital capacity is normal, as a rule. In a few instances, however, the lung capacity is sufficiently subnormal to lead one to suspect some pulmonary involvement.

In incipient pulmonary tuberculosis the vital capacity may be practically normal, even in the presence of a very active and virulent infection in the lungs.

In advanced pulmonary tuberculosis the vital capacity of the lungs is greatly reduced, in proportion to the extent of the disease process.

18. The abnormal tendency to dyspnea on exertion is much more marked when the reduced vital capacity is caused by disease of the heart, than when caused by disease of the lungs alone, even in instances where the reductions are similar in extent.

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[32] Pearce, R. G.: The Cardiorespiratory Mechanism in Health and Disease, Arch. Int. Med. **27**:139 (Feb.) 1921.

DEHYDRATION IN NEW-BORNS I *

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Since water is the medium in which the physical and chemical processes of the body take place, variations in the amount of the body fluids must be of great importance in the changes which occur during health and disease. The demonstration by Balcar and his associates [1] that fever may be produced by dehydrating animals makes the subject of particular interest in new-borns in whom fever and dehydration occur so frequently.

A number of observers believe that transient fever in the new-born is due to dehydration. This belief is based on the fact that the fever usually occurs at the time of the greatest weight loss in infants who have lost much weight. The loss of weight, it is assumed, indicates a water loss.

Objection has been raised to this conception of "inanition fever" [2] because many new-born babies lose considerable amounts of weight without developing fever while others develop fever after only slight losses of weight. In a subsequent paper we shall attempt to show that in the large majority of new-born babies with fever the plasma water is diminished. In this paper I propose to discuss the relation of weight loss to dehydration in new-born babies and to show the fallacy of drawing conclusions from the weight changes alone regarding the water content of the new-born.

The ease with which various tissues take up and lose water varies considerably. The muscles and skin apparently are very susceptible to changes in the water content of the organism. Tobler [3] dehydrated animals so that they lost from 25 to 30 per cent. of their body weight in a few days. He found that most of the water loss was accounted for by the loss in water from the muscles and skin. The blood and soft tissues lost comparatively little fluid. A number of observers [4]

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* From the Pediatric Division of the New York Nursery and Child's Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Balcar, J. D.; Sansum, W. D., and Woodyatt, R. T.: Arch. Int. Med. **24**:116 (Aug.) 1919.

2. Grulee, C. G., and Bonar, B. E.: Am. J. Dis. Child. **22**:44 (July) 1921.

3. Tobler, L.: Arch. f. exper. Path. u. Pharmakol. **62**:431, 1909.

4. Engels: Arch. f. exper. Path. u. Pharmakol. **51**:346, 1904. Bogert, L. J.; Underhill, F. P., and Mendel, L. B.: Am. J. Physiol. **41**:189, 219, 229, 1916. Smith, A. H., and Mendel, L. B.: Am. J. Physiol. **53**:323, 1920.

have also shown that when saline is injected into the vein of an animal, the fluid quickly leaves the blood going for the most part to the muscles and skin thus increasing their water content. Recently Weed and McKibben[5] found that the water content of the brain is readily varied.

For a long time it was thought that, despite variations in the water content of the tissues, the blood water remained constant. It was believed that the tissues acted as a reservoir from which water might be withdrawn and to which water might be added without significantly altering the concentration of the blood. It is now known, however, that the blood water may change under a number of conditions.[6] Rogers, in 1909,[7] using the hematocrit, found that the blood may lose more than 60 per cent. of its water in cholera. Recently Underhill and his coworkers[8] showed that, accompanying the pulmonary edema seen in war gas poisoning and influenza, the blood may become concentrated. Numerous observations also show that in acute intestinal intoxication in infants the blood may become markedly concentrated.

When an organism loses water it does not lose it uniformly from all the organs. Certain organs (muscle, skin, brain) apparently give up water very readily, while others, such as the blood and soft tissues, remain comparatively unchanged until the water loss becomes marked. In some instances, however, fairly wide fluctuations may occur in the plasma water without corresponding changes in the water content of the baby.[9]

Fairly accurate methods are available for determining changes in the water percentage of the blood and plasma. Variations in the red cell content of the blood (also hemoglobin, dry residue of the blood, corpuscular volume, etc.) indicate changes in the percentage of water of whole blood. Variations in the plasma protein per cent. indicate changes in the plasma water per cent. The total plasma volume may also be determined. Since the red cell content of the blood during the first two weeks of life varies rapidly, due to causes other than changes in the blood water, determinations of the red cells, hemoglomin, etc., are of little value as indices of changes in the blood water content.

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[5] Weed, F. S., and McKibben, L. H.: Am. J. Physiol. **48**:531, 1919.

[6] Cushing, H., and Foley, F. E. B.: Proc. Soc. Exper. Biol. & Med. **17**: 1580, 1920.

[7] Rogers, L.: Philippine J. Sc. **4**:99, 1909.

[8] Underhill, F. P.: Arch. Int. Med. **23**:753 (June) 1919. Underhill, F. P., and Ringer, M.: J. A. M. A. **75**:1531 (Dec. 4) 1920.

[9] For example, in a baby weighing 3,600 gm., 100 c.c. of saline by mouth reduced the serum protein per cent. from 7.55 to 5.93, indicating an increase of 27 per cent. in the plasma water. The amount of fluid given was only 3 per cent. of the body weight. In order to produce a corresponding increase in the water content of the rest of the tissues it would have been necessary to give nearly a liter of fluid.

In our experiments the refractive index of serum was used to measure changes in plasma water. Since, under most conditions, the plasma proteins are fairly constant, any change in their concentration is taken to indicate a change in the plasma water. The consistent results obtained in these experiments seem to indicate that in the newborn baby this assumption is, in the main, justified.

Method.—The serum protein percentage was determined with the Abbe refractometer. Distilled water was read with each series of readings. The factor for the nonproteins, determined in older infants [10] by the method of Robertson [11] was used. The calculation of the serum protein per cent. was made according to Reiss.[12]

The serum protein percentage is of importance not only because it measures changes in plasma water but also because it gives a measure of the osmotic resistance to the passage of water from the blood. The capillary wall acts as a semipermeable membrane [13] through which water and crystalloids (salts, sugar, urea, etc.) may pass freely but through which colloids are unable to pass. (In special situations, notably the liver, the plasma proteins are able to pass through the capillary wall, but in the main, Bayliss believes, the capillaries are impermeable to colloids). These colloids, the plasma proteins mainly, exert an osmotic pull on water which, according to Starling [14] amounts to from 30 to 35 mm. of mercury.

In the capillary we have, therefore, a force, the blood pressure, tending to squeeze water out of the circulation, while opposing it is the osmotic pressure of the plasma proteins which tends to hold water in the capillaries. One can readily understand that an increase in the plasma protein concentration, whether due to a diminution in the plasma water or to an actual increase in the plasma proteins, results in an increase in the resistance to the passage of water from the capillaries.

It is possible that the refractive index of the serum of the newborn baby gives only a rough estimate of the protein concentration of plasma. Lewis and Wells [15] have shown that in the serum of newborns euglobulin is almost entirely absent. The use of the factor 0.00172 (Reiss) for the calculation of the serum proteins is based on the assumption that the serum globulin and serum albumin exist in the same proportion as in the serum of adults. However, though the absolute values may not be correct, the relative differences of concentration are sufficiently large so that the significance of the results is in no way diminished.

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[10] Bakwin, H.: Am. J. Physiol. **60**:343, 1922.

[11] Robertson, T. B.: J. Biol. Chem. **22**:233, 1915.

[12] Reiss, E.: Ergebn. d. inn. Med. u. Kinderh. **10**:531, 1913.

[13] Bayliss, W.: J. Pharmacol. & Exper. Therap. **15**:29, 1920.

[14] Starling: J. Physiol. **19**:312, 1896.

[15] Lewis, J., and Wells, H. G.: J. A. M. A. **78**:863 (March 25) 1922.

For purposes of comparison a chart showing the serum protein concentration of babies during the first week of life is shown(Fig. 1). Only afebrile babies are represented. It will be seen that the serum protein per cent. is usually between 6 and 7. It rises only rarely above 7.5, and in but three instances did it rise above 8. After the fourth day it is unusual to find the serum proteins above 7 per cent.

Hemoglobin was determined by the Palmer method.[16] The carbon monoxid standard was checked repeatedly with the Van Slyke and Stadie method[17] over a period of several months and found to check within 2 per cent. The hemoglobin results are charted in grams per hundred cubic centimeters of blood.

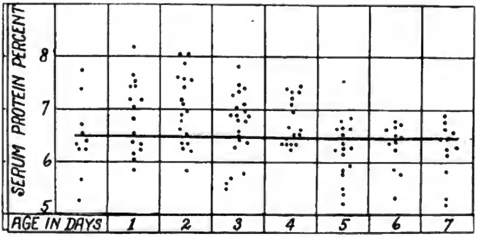

Fig. 1.—The serum protein per cent. of babies during the first week of life. The dots represent the individual determinations, the heavy black line the average serum protein per cent. Most of the points lie between 6 and 7 per cent., rarely above 7.5 per cent.

A loss of skin elasticity indicates that the water content of the skin is diminished below normal. In this discussion the degree of inelasticity has been designated by the number of pluses, 1 plus indicating a slight but distinct diminution in skin elasticity, 2 plus a more marked degree of inelasticity, etc.

THE RELATION BETWEEN CHANGES IN WEIGHT AND CHANGES IN THE WATER CONTENT OF THE NEW-BORN BABY

There are no direct methods for measuring variations in the water content of the tissues during life. The only indications of such changes are variations in the body weight and the condition of the skin. Freund[18] showed that the daily up and down curve of an infant's weight is largely accounted for by changes in the water content of the organism. In the new-born a number of factors must be considered in estimating the significance of weight changes. The meconium, urine in the bladder, regurgitated allantoic fluid and vernix caseosa account for some of the weight loss. A part of it is also due to an actual loss of body tissue or stored food reserve during the starvation. This loss, according to Benedict and Talbot[19] amounts to about 17 gm. of fat per day for a baby weighing 3.76 kg. (from 35 to 40 gm. of protein or carbohydrate). The rest of the weight loss is due to water. For example, if a baby loses 300 gm. during the first three days of life, a not usually large loss, about 100 gm. are due to the loss of weight from meconium, etc.,[20] about 115 gm. at most, are due to loss of tissue or food reserve and the remaining 85 gm. are due to water loss. Since most infants get some food during this time from the breast, and, at the New York Nursery and Child's Hospital, from whey which is given after each breast feeding, the water loss is probably considerably greater than the rough calculations just given indicate. It seems reasonable to assume, therefore, that the weight loss gives a rough index of the water loss in a new-born baby.

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[16] Palmer, W. W.: J. Biol. Chem. **33**:119, 1918.

[17] Van Slyke, D. D., and Stadie, W. J.: J. Biol. Chem. **49**:1, 1921.

[18] Freund, W.: Jahrb. f. Kinderh. **59**:421, 1904.

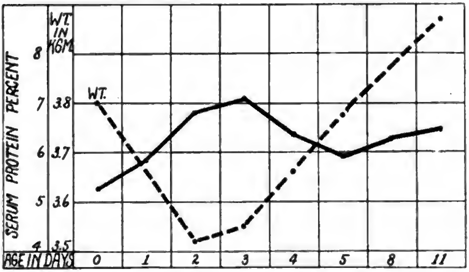

Fig. 2.—Case 1. Increase in serum protein per cent. accompanying the loss of weight after birth. The serum proteins at birth were 5.23 per cent. Accompanying the loss of 280 gm. the serum proteins rose on the third day to 7.09. With the increase in weight between the third and fourth days the serum proteins fell to normal and remained there during the rest of the period of observation.

Variations in the Water Content of Babies at Birth.—In estimating the significance of weight changes in regard to the water content of the new-born baby at any particular time, it is essential that the water

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19. Benedict, F., and Talbot, F.: Carnegie Institution, Publication No. 233, 1915, p.11.

20. Vierordt-Gerhardt: Handbuch für Kinderkrankheiten **1**:118, 1877; quoted by Griffith: Diseases of Children, Philadelphia **1**:46, 1921.

content of the baby at birth be considered. For example, a baby who has a large water reserve at birth can lose a great deal more weight without becoming dehydrated than can another infant who is dehydrated at birth.

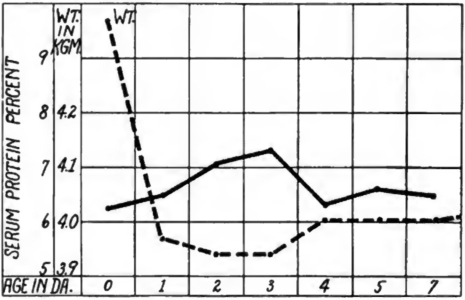

Fig. 3.—Case 2. Increase in the serum proteins accompanying the loss of weight after birth. In this baby the loss of 430 gm. was accompanied by a rise of the serum proteins from 6.28 to 7.31 per cent. With the increase in weight the serum protein concentration dropped to normal and remained there.

TABLE 1.—Dehydration Accompanying the Loss of Weight After Birth

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
1 (Fig. 2)	Birth	3,800	5.23	....	Normal
	1	.....	5.87	....	1 plus, inelastic
	2	3,520	6.80	....	1 plus, inelastic
	3	3,520	7.09	....	1 plus, inelastic
	4	3,660	6.34	....	Normal
	5	3,750	5.93	....	Normal
	8	.....	6.28	....	Normal
	11	3,970	6.45	....	Normal
2 (Fig. 3)	Birth	4,370	6.28	18.3	Normal
	1	3,970	6.51	17.8	1 plus, inelastic
	2	3,940	7.09	19.2	1 plus, inelastic
	3	3,940	7.31	17.2	1 plus, inelastic; Temp. in a.m. 38 C.
	4	4,040	6.34		
	5	4,010	6.62	20.3	Normal
	7	4,040	6.45	....	Normal

The case reports show that the water content of the baby at birth may vary widely. Usually, as the baby loses weight during the first few days after birth, the skin becomes inelastic and the plasma concentration increases indicating a diminution in skin and plasma water (Table 1).

Two babies (Cases 1 and 2) showed no evidence of dehydration at birth. The skin turgor was good and the plasma concentration (serum protein per cent.) not increased. During the first three days of life they lost considerable amounts of weight. The weight loss was accompanied by an increase in the plasma concentration and a loss of skin elasticity (diminution of plasma and skin water). As the babies started to gain the blood and skin returned to normal.

An increase in the serum protein concentration during the loss of weight after birth has been noted by Rott[21] and by Rusz.[22] The hemoglobin per cent. in Case 2 varied from day to day without relation to weight or serum protein per cent.

There are babies, however, who apparently are born with a large water reserve. In these babies the weight loss is unaccompanied by any detectable evidence of dehydration (Table 2). Such cases have been described by Utheim.[23] Two babies (Cases 3 and 4) lost considerable amounts of weight without showing any evidence of skin or plasma dehydration. It is possible that the water reserve was large at birth, or that the water lost came from the deeper tissues such as the muscles, etc., where it could not be detected by the methods employed. It is possible that the weight loss was accompanied by a destruction of the plasma proteins so that a diminution in the plasma water might have occurred which was compensated for by a loss of plasma protein. The fact that the skin as well as the plasma did not become dehydrated, despite the weight loss, seems to indicate that the water reserve in these babies was large at the start. Whatever the explanation for the failure of the plasma to become concentrated, however, the fact remains that, in spite of the loss of considerable amounts of weight in certain babies, the serum protein concentration remains normal. This is of considerable importance in view of the close rela-

TABLE 2.—Loss of Weight Unaccompanied by Dehydration

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
3	Birth	3,150	6.57	22.3	Normal
	1	2,980	6.39	19.8	Normal
	2	2,840	6.28	20.5	Normal
	3	2,810	5.75	....	Edema of dorsum of hand and feet
	4	2,810	....	19.9	Normal
	5	2,770	5.40	19.2	Normal
	6	2,840	5.87	....	Normal
4	Birth	3,840			
	1	3,780	6.34	....	Normal
	2	3,580	6.68	....	Normal
	3	3,580	6.51	....	Normal
	5	3,600	5.64	....	Normal
	7	3,600	6.16	....	Normal
	11	3,090	0.11	....	Normal

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21. Rott, F.: Ztschr. f. Kinderh. (Originalien) **1**:43, 1910.
22. Rusz, E.: Monatschr. f. Kinderh. (Originalien) **10**:360, 1912.
23. Utheim, K.: Saertryk av Norsk Mag. f. Lægevidensk., 1921, p. 104.

tionship between fever in the new-born and an increase in the serum concentration.

In the two cases just described the weight loss was unaccompanied by any evidence of dehydration, probably because the babies had large water reserves at birth. There are babies, however, who are dehydrated at birth. In one of the babies referred to the skin alone was involved; in the two others, the skin and plasma. Case 5 was first observed fifteen hours after birth (first day). At this time the skin was dry and inelastic, indicating a diminution in skin water. The plasma water was normal. As the baby lost weight the plasma quickly became concentrated. With the increase in weight on the fifth day the plasma returned to normal. The skin, however, remained dehydrated for several days afterward. Case 6 was observed three hours after birth; another baby (Case 7) was seen thirteen hours after birth. During this time the latter had lost 30 gm., an insignificant loss in weight and hardly sufficient to account for the dehydration. At the first observation both showed distinct evidence of skin and plasma dehydration as indicated by the marked skin inelasticity and the high serum protein concentration. At this time they were more dehydrated than most of the afebrile babies who had lost large amounts of weight.

TABLE 3.—SKIN DEHYDRATION AT BIRTH

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
5	Birth	3,750			
	1	3,750	6.16	19.2	2 plus, inelastic, dry
	2	3,490	7.14	22.1	2 plus, inelastic, dry
	3	.....	....	20.7	2 plus, inelastic, dry
	4	3,440	7.31	20.3	2 plus, inelastic, dry
	5	3,490	6.63	21.0	2 plus, inelastic, dry
	6	3,550	6.28	21.3	2 plus, inelastic, dry
	8	3,580	6.86	19.6	Doubtful
	12	3,600	6.57	....	Normal

TABLE 4.—SKIN AND PLASMA DEHYDRATION AT BIRTH

Case	Age, Days	Weight, Gm.	Serum Protein, %	Skin
6	Birth	2,950	7.43	3 plus, inelastic, dry
	1	2,890	7.61	3 plus, inelastic, dry
	2	.....	8.02	3 plus, inelastic, dry
	3	2,890	6.91	3 plus, inelastic, dry
	4	3,010	6.97	3 plus, inelastic, dry
	6	3,130	6.61	Normal
	12	3,290	6.51	Normal
7	Birth	3,320		
	1	3,290	7.48	3 plus, inelastic, dry
	2	3,290	8.06	2 plus, inelastic, dry
	3	3,140	7.48	2 plus, inelastic, dry
	4	3,140	7.20	3 plus, inelastic, dry
	6	3,260	7.55	Dry, no loss of elasticity
	8	3,320	6.74	Normal

The desiccation persisted as long as the babies continued to lose weight. In Case 6 the serum protein concentration returned to normal two days before the skin. In Case 7 the skin regained its elasticity before the plasma water had returned to normal.

At birth, apparently, the water content of the baby may show many degrees of variation. At one extreme is the watery baby who may lose considerable amounts of weight without showing any evidence of dehydration. At the other extreme is the dried out, desiccated baby who at birth shows a dry, inelastic skin and a concentrated plasma. Between these two extremes all gradations exist.

Increase in the Plasma Water Without Increase in Weight.—Another point to be considered in estimating the significance of weight changes in regard to the water content of the baby is the transportation of water in the baby from one tissue to another. In a few instances we have noted a fall in the serum protein concentration from one day to another without any increase in weight.

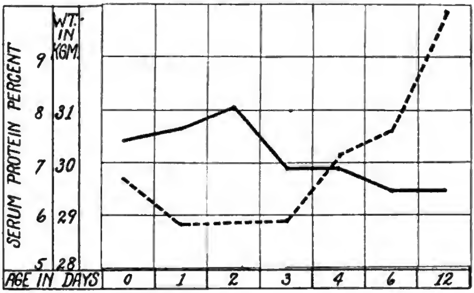

Fig. 4.—Case 6. Dehydration at birth. On the birthday the serum protein per cent. was 7.43 per cent., indicating a concentrated plasma. A loss of a few grams was accompanied by a rise of the serum proteins to 8.02 per cent., a high figure rarely reached by afebrile babies. Between the third and fourth days the serum proteins fell to 6.91 and remained normal thereafter.

In two babies (Cases 8 and 9) the plasma became more watery despite the fact that the weight did not increase. The decrease in the plasma concentration may have been due to an increase in plasma water or to a destruction of plasma proteins. Whatever the explanation, however, the fact remains that an increase in the plasma water per cent. may occur without any increase in weight.

The Relation Between Skin and Plasma Water in the New-Born.—When dehydration develops in a new-born baby it is usual for the skin to lose its elasticity before the plasma has become concentrated and to persist for some time after the plasma water has returned to normal (Cases 1, 2, 5 and 6). It is not at all unusual to find the skin inelastic in a baby whose plasma is normal or even dilute (Case 1, second day). Marked degrees of skin inelasticity are usually accompanied by an increase in the plasma concentration although this is by no means always the rule (Case 6).

TABLE 5.—Increase in Plasma Water Without Change of Weight

Case	Age, Days	Weight, Gm.	Serum Protein, %	Hemoglobin, Gm. per 100 C.c.	Skin
8	Birth	3,260			
	1				
	2	3,180			
	3	3,120	....	7.3	1 plus, inelastic
	4	3,120	8.49	15.9	1 plus, inelastic
	5	3,120	6.91		
	6	3,120	6.57	15.6	Normal
	7	3,120	6.57	....	Normal
9	Birth	3,690			
	1	3,690	8.49	....	1 plus, inelastic, dry
	2	3,630	7.31	....	2 plus, inelastic, dry
	3	3,630			
	4	3,690			
	5	3,750			

An increase in the plasma concentration is usually accompanied by a loss of skin elasticity. In a few instances the skin was normal while the plasma was concentrated (Case 7, sixth day). In one baby with a serum protein per cent. of 9.40, the skin, although very loose, showed no evidence of dehydration. In the fever cases, particularly, the plasma may be markedly dehydrated with only slight impairment of the skin elasticity.

The Relation Between Hemoglobin Per Cent. and the Water Content of the New-Born Baby.—In a number of cases, daily determinations of the hemoglobin were made. No relation, however, was found between the weight changes, serum protein percentage and the hemoglobin.

SUMMARY AND CONCLUSIONS

1. Dehydration was studied in new-born babies by correlating weight changes, skin elasticity and serum protein concentration (plasma water).

2. Uusually a marked weight loss in the new-born baby is accompanied by a loss of skin elasticity and an increase in the serum concentration (indicating a diminution in skin and plasma water).

3. There are babies, however, who, despite relatively large weight losses, show no evidence of dehydration of the skin or plasma In these babies, presumably, the water reserve of the tissues at birth is large.

4. On the other hand, there are babies who show evidence of dehydration at birth. The skin alone may be desiccated (loss of skin elasticity without increase in the serum protein concentration) or both skin and plasma may be involved (loss of skin elasticity and increase in serum protein concentration).

5. Since the water content of the baby varies so widely at birth it is impossible to tell from the weight curve alone whether or not a baby is dehydrated.

6. The plasma water per cent. may increase even though there is no increase in weight.

7. Impairment of skin elasticity may, and often does, occur without increase in the plasma concentration. Increase in the plasma concentration is usually, but not always, accompanied by an inelastic skin.

It is with pleasure that I acknowledge my indebtedness to Dr. H. M. Painter and Dr. Fellows Davis, Jr., for the use of material from the Obstetrical Service of the New York Nursery and Child's Hospital. I wish to thank Dr. J. F. Sammis and Dr. L. C. Schroeder for their stimulating interest in the work. Thanks are due to Dr. Donald McGill, Resident, for his cooperation and to Miss Ethel Viele for her valuable assistance.

DEHYDRATION FEVER IN NEW-BORNS II *

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The frequent occurrence of a transient fever during the first few days of life is now generally recognized. The exact nature of the fever has not yet been satisfactorily explained. Holt,[1] who gave the first adequate description of the condition in 1895 ascribed it to starvation and called it inanition fever.

Of the many hypotheses which have been advanced to explain this peculiar fever the one which has received the most experimental support is that which attempts to explain the fever as due to water loss. The observation originally made by Holt that the fever usually occurs at the time when the weight loss is greatest and disappears when the baby starts to gain has been amply confirmed.[2] Holt also showed that the fever can be made to disappear by administering fluids.[3] He mentions instances of fever in older infants on low fluid intakes which cleared up when fluid was given. Stewart[4] succeded in reducing the incidence of fever in new-borns by giving lactose solutions between nursings. Faber[5] practically prevented fever in new-borns by complemental feedings of whole milk dilutions.

In 1910, Erich Mueller[6] described two cases of fever in older infants who were receiving very little fluid. In both instances the temperature fell to normal when fluids were given. Grulee and Bonar[7] described similar instances of fever in infants who were receiving concentrated diets. In these babies, as in Mueller's, the fever disappeared when fluids were given. In one of their babies the red cell content of the blood was high during the fever falling after the temperature had become normal. They interpreted the high red cell count as indicating a diminution in the blood water. Marriott[8] has suggested that the fever which occurs so frequently in babies with severe diarrhea may be due to dehydration.

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[1] Holt, L. E.: Arch. Pediat. **12**:560, 1895.

[2] Von Reuss, A. R.: Ztschr. f. Kinderh. (Originalien) **4**:32, 1912. Heller, F.: Ztschr. f. Kinderh. (Originalien) **4**:55, 1912.

[3] See also Peteri, I.: Jahrb. f. Kinderh. **80**:612, 1914.

[4] Stewart, C. A.: J. A. M. A. **78**:1865 (June 17) 1922.

[5] Faber, H. K.: Am. J. Dis. Child. **24**:56 (July) 1922.

[6] Mueller, E.: Berl. klin. Wchnschr. **47**:673, 1910.

[7] Grulee, C. G., and Bonar, B. E.: Am. J. Dis. Child. **21**:220 (March) 1921.

[8] Marriott, W. M.: Harvey Lectures, 1920.

In 1915, Balcar, Sansum and Woodyatt[9] produced marked degrees of fever in animals by severely dehydrating them with intravenous injections of hypertonic glucose solutions given rapidly. They suggested that the fever was due to a failure of normal heat loss because of lack of water evaporation from the body.

Barbour and Howard[10] showed that the fall in temperature following the administration of glucose to dogs with fever is accompanied by a hemodilution (decrease in the hemoglobin per cent. of the blood). They also found that in colon bacillus fever in animals and in human febrile cases antipyrin, quinin and salicylates reduce the blood concentration. Schmitt and Sansum[11] succeeded in reducing the temperature of patients with pneumonia and influenza several degrees and in some instances below 37.8 C. (100 F.) by giving large quantities of fluid by mouth. In a recent review Barbour[12] strongly favors the view that "body temperature is regulated by water shifting under nervous control."

The investigations described in this paper were undertaken in an attempt to determine the relationship between dehydration and fever in the new-born. Three methods were used for estimating dehydration, the plasma concentration (refractive index of serum), the condition of the skin and the weight loss.

The applicability of these methods to a study of dehydration in the new-born has been discussed in the previous paper.[13] It was pointed out that the water content of babies at birth varies widely. Usually a distinct weight loss during the first days after birth is accompanied by a loss of skin elasticity and an increase in the plasma concentration indicating a loss of water from the skin and plasma. In some babies, however, comparatively large weight losses occur without the development of skin or plasma dehydration. In these babies, presumably, the water reserve at birth is large. On the other hand, some babies at birth show evidence of skin and plasma dehydration (loss of skin elasticity and increase in serum protein concentration). From the weight curve alone, therefore, one cannot draw conclusions as to the water content of the new-born baby; the water content of the baby at birth must also be considered. This variation in the water content of the baby at birth explains the occurrence of dehydration fever in new-borns without very large weight losses (dehydration at birth).

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[9] Balcar, J. O.; Sansum, W. D., and Woodyatt, R. T.: Arch. Int. Med. **24**:116 (July) 1919.

[10] Barbour, H. G., and Howard, A. J.: Proc. Soc. Exper. Biol. and Med. **17**:150, 1920.

[11] Schmitt, E. C., and Sansum, W. D.: Cal. State J. Med. **19**:371, 1921.

[12] Barbour, H. G.: Physiol. Rev. **1**:295, 1921.

[13] Bakwin, H.: Am. J. Dis. Child. **24**: (Dec.) 1922.

It also explains the lack of fever in certain babies who lose a great deal of weight (large water content at birth).

Procedure and Methods.—Daily determinations were made on a group of normal and febrile babies. Blood for refractive index (and in a number of cases for hemoglobin) was drawn from the toe without pressure from three to four hours after a feeding. The temperature of the baby was taken at the time of the puncture. Details of the technic for the serum protein (refractive index of serum) and hemoglobin determinations are given elsewhere.[13]

The only study recorded in the literature on the plasma water in new-born babies with fever is that of Utheim.[14] She concluded that fever in the new-born may occur without a simultaneous increase in the concentration of the plasma. The refractometric method was used.

According to Reiss [15] in older infants with fever due to various infections, the plasma is more dilute than normal (refractometric determination of serum). A large number of determinations made in this laboratory during the past three years showed no increase in the serum protein concentration during the fever associated with various infections. We have had little opportunity to study the plasma concentration in new-borns with fever due to infections. In one baby 5 days old with sepsis and a temperature of 40.6 C. (105 F.) the serum protein was low—5.87 per cent. In another new-born baby with diarrhea and a temperature of 38.3 C. (101 F.) the serum protein was 6 per cent., which is a low normal.

Observations were made on fifty new-borns with fever. Of these, one case each of sepsis, diarrhea and hemorrhagic disease have not been used in the preparation of Figure 1. In these cases the serum protein concentration was not increased. The remaining forty-seven cases with which this paper concerns itself conformed fairly closely to the classical description of inanition fever. The fever usually occurred from forty-eight to ninety-six hours after birth in babies who had lost considerable amounts of weight. In some of the babies, however, the onset of the fever was within the first thirty-six hours after birth and in some the weight loss was not marked.

The skin usually showed some evidence of dehydration (dry, inelastic skin). In most instances this was not more marked than in the afebrile babies. The association between fever in new-borns and a loss of skin elasticity is not a close one. Some of the babies, particularly those with a high serum concentrations, appeared to be quite ill. They were prostrated, apathetic, limp and at times looked pale. Other babies, however, with equally high serum concentrations did not appear ill.

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14. Utheim, K.: Saertryk av Norsk. Mag. f. Laegev., 1921, p. 104.
15. Reiss, E.: Ergebn. d. inn. Med. u. Kinderh. **10**:531, 1913.

In Figure 1 are shown the results of serum protein determinations on normal and febrile babies. The dots represent the afebrile babies, the crosses the febrile. The lower line represents the average normal serum protein percentages each day; the upper line the average for the febrile babies. The serum protein per cent. of normal new-borns lies fairly constantly between 6 and 7. In only three of the babies did it rise above 8 per cent. In the febrile babies the serum protein was usually above 7.5 per cent. In five babies it rose above 9 per cent., as high a figure as is seen in many severe cases of acute intestinal intoxication in older infants. These results show that in the group of cases of fever studied the plasma concentration was definitely increased.

In eight babies the serum proteins did not rise above 7 per cent. during the fever. In five of these the fever was associated with a febrile affection in the mother. It seems possible that a pyrogenetic substance may be transmitted from mother to baby in these cases (Cases 7 and 8). In Case 8 mother and baby had fever at varying times for twenty-seven days after the delivery (Fig. 8). There is fairly close parallelism between rises in the temperature of the mother and baby. The baby's serum protein concentration on the second day of life, when the temperature was 40.7 C. (105.2 F.) was 6.97 per cent., which is within normal limits. In Case 7 the temperature of the mother rose at the same time as the baby's. The baby's temperature remained elevated until it was weaned on the sixth day. In this case also, the serum proteins were not increased.

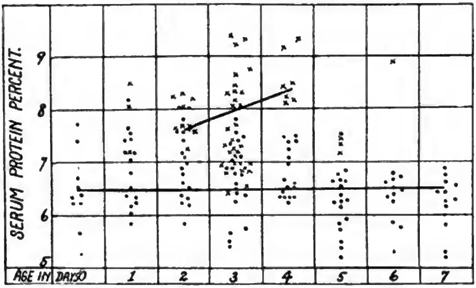

Fig. 1.—The serum protein per cent. in dehydration fever in new-borns. Dots, normal babies; crosses, febrile babies. Upper black line, average for febrile babies; lower black line, average for normal babies.

In Table 1 are shown the weight losses and the serum protein percentages (plasma concentration) of a group of normal and febrile babies. The weight losses in babies with dehydration fever vary from 60 to 700 gm., averaging 350 gm. In the normal babies the weight losses varied from 120 to 540 gm., averaging 280 gm. It will be seen that fever, though more common in babies who had lost a great deal of weight, nevertheless occurred in babies who had lost only small amounts. In these latter babies, however, the increase in serum concentration was as marked as in babies who had lost larger amounts of weight. Losses of weight, therefore, are of significance in relation to fever in the new-born only as they affect the plasma concentration. Since the water content of the baby varies so widely at birth, the weight loss, except perhaps when marked, gives but a poor index of the water content of the plasma.

TABLE 1.—THE WEIGHT LOSS AND THE SERUM PROTEIN PERCENTAGE IN NORMAL AND FEBRILE BABIES

Normal Babies		Febrile Babies	
Weight Loss, Gm.	Serum Protein, per Cent.	Weight Loss, Gm.	Serum Protein, per Cent.
		700	9.40
		660	8.96
		660	8.37
		620	8.49
		600	7.84
540	7.43	540	8.30
		510	8.61
450	6.22	480	7.73
430	7.31	450	8.89
420	6.39	450	8.02
420	7.33		
390	6.16	360	8.24
390	7.37	360	7.26
330	7.31	360	8.73
310	6.28	330	7.14
300	6.51	310	7.26
		300	8.89
		300	7.26
280	6.80	210	9.19
270	7.84		
240	5.69		
240	6.86		
200	6.34		
180	6.91	180	7.31
180	6.57	180	8.02
180	7.48	150	8.49
180	6.39		
150	7.09		
120	6.29		
		90	8.13
		60	8.49

The hemoglobin varied from day to day without relation to fever, weight or changes in the serum protein per cent. Though there is no relation between variations in the hemoglobin and fever, it is possible that the high red cell content of the blood of new-born babies, by increasing the blood viscosity and thereby slowing the peripheral blood flow, might tend to diminish heat loss and hence make the occurrence of fever more likely.

Comment.—During recent years a considerable amount of evidence has accumulated showing that a close relationship exists between fever and water shifting. In our studies on fever in the new-born, a large proportion of the cases showed a well marked increase in the serum protein per cent., indicating a diminution in plasma water. The concentration of the serum proteins was often as marked as is seen in infants with acute intestinal intoxication. The drop in temperature was accompanied by a well marked drop in the serum concentration. Though the serum of afebrile babies also became concentrated during the loss of weight which occurs in the first three or four days of life, this was rarely as marked as in the febrile babies. Similar increases in the serum concentration are not found in babies with fever due to various infections. It seems clear, therefore, that the cases of fever in new-borns differ from the fevers due to infections in that they are associated with a diminution in the plasma water.

Confirmatory evidence of the close relationship between dehydration and these cases of fever is found in the readiness with which the fever can be reduced by giving fluids. In a number of instances water or glucose solution, warmed to a temperature above that of the baby, was given by gavage. In the large majority of cases so treated the temperature fell several degrees in from thirty to sixty minutes after the gavage.

It seems probable that other factors contribute to the ease with which new-born babies develop fever. It is not unlikely that the high red cell content of the blood, by increasing the viscosity, slows the rate of blood flow and thus diminishes heat elimination.

In the two cases mentioned infections in the nursing mother were associated with fever in the baby. In these babies the serum protein concentration was not increased. It is conceivable that minor disturbances in the mother which pass undetected may also be factors in predisposing, or in some instances causing, fever in the new-born baby.

SUMMARY OF CONCLUSIONS

1. A group of cases has been described in which fever in the new-born baby was associated with a diminution in the plasma water (increase in the serum protein concentration). The fall in temperature was coincident with an increase in the plasma water.

2. A similar increase in the serum concentration is not found in normal new-borns nor in babies in whom fever is due to other causes.

REPORT OF CASES

The following case reports illustrate the close relationship between fever in the new-born baby and the plasma water. Two cases in which fever in the baby was associated with fever in the mother are also shown.

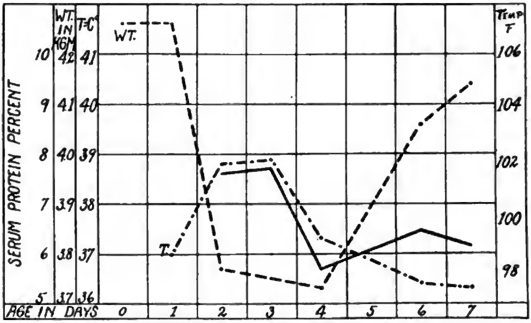

Fig. 2 (Case 1).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in dehydration fever. The loss of weight is accompanied by a rise of temperature and an increase in the serum protein per cent. The temperature and serum protein per cent. fall on the fourth day and remain normal thereafter.

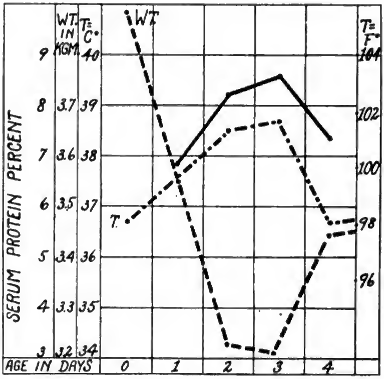

Fig. 3 (Case 2).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in dehydration fever. In this case a marked loss in weight is accompanied by a rise of temperature and an increase in the serum protein per cent. The temperature and increased serum concentration persist until the weight gain starts on the fourth day, after which they are normal.

CASE 1 (Fig. 2).—*Dehydration Fever.*—The mother was a primipara, aged 26. Labor was normal. On the afternoon of the delivery the temperature rose to 38.5 C. (101.2 F), but after this it was normal.

At birth the baby weighed 4,260 gm. and was apparently vigorous. During the first two days after birth he lost 490 gm. The temperature, which up to that time had been normal, rose to 38.8 C. (101.8 F.). The patient seemed well otherwise, except that the skin was 2 plus inelastic. The serum protein concentration was 7.61 per cent., indicating a diminution in the plasma water. The fever and hehydration (loss of skin elasticity and increased serum protein concentration) persisted on the third day. On the fourth day, the temperature fell to normal, and at the same time the serum protein per cent. dropped from 7.70 to 5.70 per cent. The baby continued to gain well after this, and the serum protein per cent. remainded normal during the rest of the period of observation.

CASE 2 (Fig. 3).—*Dehydration Fever. Reduction in Temperature and Serum Concentration Following the Administration of Fluids.*—The mother was a primipara, aged 24. The delivery and postpartum course were normal without fever.

The baby weighed 3,880 gm. at birth and seemed to be vigorous. When first observed, twenty-three hours after birth, he had lost 280 gm. The temperature was normal, and there was no evidence of skin or plasma dehydration. The baby continued to lose weight, and by the second day had lost a total of 540 gm. On this day his temperature rose to 38.5 C. (101.4 F.). The skin was slightly inelastic (1 plus), and the serum proteins had risen from 6.86 on the first day to 8.20 on the second. The fever persisted on the third day, the skin and plasma remaining dehydrated. Between the second and third days there was a further loss of 80 gm.

During the night following the third day the patient was given an ounce of 5 per cent. glucose solution, every two hours, in addition to the regular breast feeding. On the fourth day his weight had increased 230 gm. The temperature was normal, and the serum protein per cent. dropped from 8.60 on the third day to 7.31 on the fourth day. The baby continued normally after the fourth day.

CASE 3 (Fig. 4).—*Dehydration Fever Occurring Within Thirteen Hours After Birth.*—This was the mother's second pregnancy. The first child, a girl, was 3 years old and quite well. The postpartum course was normal except for fever and pain in the lower abdomen on the fourth day postpartum.

The patient weighed 3,800 gm. at birth. He was first seen thirteen hours after birth. He had lost 190 gm., the skin was slightly inelastic (1 plus), and the temperature, which was normal at the time of birth, had risen to 38.7 C. (101.8 F.). On the next day the temperature had risen still further, to 40.2 C. (104.2 F.), and the patient had lost an additional 150 gm. By the next day (third day) the baby had gained 90 gm., the temperature had fallen to normal, and he continued afebrile after this. During the fever the serum protein per cent. was increased, falling on the third day with the subsidence of the fever. The baby's temperature rose and fell before the mother's indisposition on the fourth day.

CASE 4.—*Dehydration Fever with Marked Increase in Serum Protein Concentration.*—The mother was a primipara, aged 28. The labor was prolonged and high forceps were applied under ether anesthesia. A large baby weighing 4,430 gm. was delivered. The mother's temperature was about 37.8 C. (100 F.) for the first three days after delivery, after which it rose to 39.5 C. (103 F.). On the fifth day, a small pelvic abscess was opened and drained, and the temperature gradually fell, reaching normal on the twelfth day. The mother left the hospital on the seventeenth day feeling well.

The baby weighed 4,430 gm. at birth. During the first three days after birth he lost 550 gm. His temperature, which up to the third day had been normal, rose to 39.7 C. (103.4 F.). The skin was very loose, but not inelastic.

The serum protein concentration was 9.10 per cent., rising later in the day to 9.40. The baby continued to lose weight between the third and fourth days, losing a total of 700 gm. The temperature was still elevated (39.2 C.) and the serum proteins were 9.30 per cent.

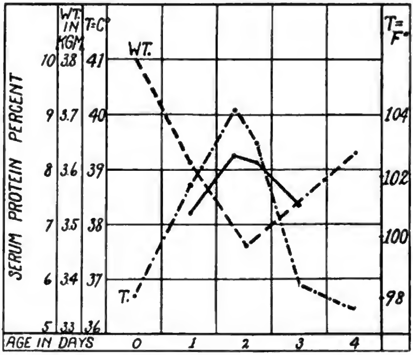

Fig. 4 (Case 3).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in dehydration fever. The loss of weight is accompanied by a rise of temperature and an increase in the serum protein per cent. The temperature and serum proteins fall on the third day as the weight gain starts. In this baby the fever occurred within thirteen hours after birth.

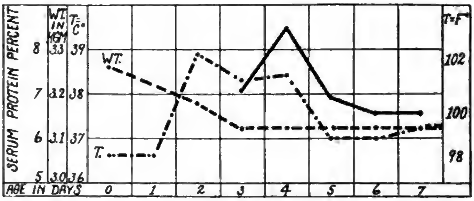

Fig. 5 (Case 5).—Dehydration fever in a new-born baby who has lost only 90 gm. The loss of a few grams is accompanied by a rise of temperature and an increased serum protein concentration. The temperature falls at the same time as the serum proteins.

On the fifth day the temperature dropped to 38 C. (100.4 F.). The serum proteins fell to 8.50 per cent. and the weight increased 60 gm. On the sixth day the temperature fell to normal, and remained there during the remainder of the baby's stay in the hospital. The serum proteins also fell from 8.50 on the fifth day to 7.30 on the sixth day, after which observations were discontinued.

Case 5 (Fig. 5).—*Dehydration Fever Unassociated With a Large Weight Loss.*—The mother was a primipara, aged 22. Delivery was instrumental (median forceps). The mother's temperature was normal until the fifth day postpartum, when it rose to 38.3 C. (101 F.), after which it remained elevated until the thirteenth day. It then dropped to normal and remained there until the mother's discharge from the hospital on the twentieth day postpartum.

The baby weighed 3,260 gm. at birth. Nothing abnormal was noted until the second day after delivery, when the baby's temperature rose to 38.9 C. (102.2 F.). He had lost only 80 gm. The patient was first seen on the following day (third day). He had lost an additional 60 gm. (total loss, 140 gm.); his temperature was 38.3 C. (101 F.), and the skin and plasma were dehydrated (serum protein per cent., 7.09). On the next day the fever persisted, the serum protein per cent. rising to 8.49. Between the fourth and fifth days, the temperature and serum protein per cent. fell to normal. There was no increase in weight. The subsequent course was normal.

Case 6 (Fig. 6).—*Severe Dehydration Fever. Fall in Temperature and Serum Concentration Following the Administration of Fluids.*—This was the mother's third pregnancy. Delivery and postpartum course were normal.

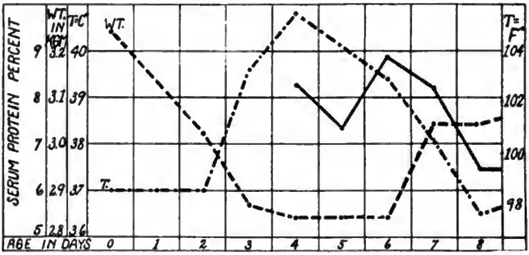

Fig. 6 (Case 6).—The relation between temperature, weight loss and serum protein per cent. (plasma concentration) in a severe case of dehydration fever. This case, like the others, shows the rise of temperature and increase in serum protein per cent. during the weight loss after birth. The serum proteins fall to normal as the temperature drops between the sixth and seventh days.

The baby weighed 3,240 gm. at birth. On the third day, after a loss of 370 gm., he developed fever which persisted until the eighth day, when it returned to normal. On the fourth day, the temperature was 40.8 C. (105.4 F.). During the febrile period the serum protein per cent. was high—8.89 on the sixth day. At this time, water was given by gavage (190 c.c.), and the nurses were instructed to give the baby water frequently during the night. On the following day (seventh day), the temperature fell to 38 C. (100.2 F.), and on the eighth day it was normal. With the fall in temperature the serum protein concentration dropped to normal, remaining there during the rest of the period of observation. The skin, which was inelastic during the fever, returned to normal, when the weight gain started between the sixth and seventh days.

Case 7 (Fig. 7).—*Fever in the Baby Associated with a Febrile Affection in the Mother. Intermittent Fever in the Baby for Twenty-Seven Days After Birth. No Increase in Serum Protein Concentration.*—The mother was a primipara, 21 years of age. Labor was normal. On the afternoon of the delivery her temperature, which had been normal in the morning, rose to 38.5 C. (101 F.), and remained elevated, with slight remissions, for thirty-four days, fluctuating between 36.8 C. (98.2 F.) and 39.1 C. (102.4 F.). She was discharged cured on the fortieth day postpartum. The diagnosis was phlebitis of the left femoral vein.

The baby weighed 3,900 gm. at birth. The temperature taken shortly after birth was 37.8 C. (100 F.). It gradually rose and on the second day was 40.7 C. (105.2 F.). By this time the baby had lost 180 gm., but the skin was normally elastic and the plasma showed no evidence of dehydration (serum protein per cent., 6.97). On the third day the temperature dropped to 38 C. (100.2 F.), the skin and plasma remaining as observed (serum protein per cent., 6.91). The temperature of the baby and mother continued to fluctuate for thirty-four days, during most of which time the baby gained well. Note the parallelism between the mother's temperature curve and the baby's (Fig. 7).

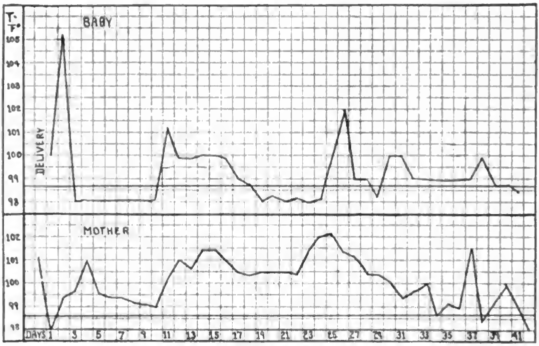

Fig. 7 (Case 7).—The relation between temperature in the mother and temperature in the baby. The upper line represents the temperature curve of the baby, the lower the temperature curve of the mother. Note the parallelism in the two curves. In this baby the serum concentration, determined on the second and third days, was normal.

TABLE 2 (Case 8).—Fever in the Baby Associated with a Febrile Affection in the Mother

Baby						Mother	
Age, Days	Weight, Gm.	Temperature, C.	Serum Protein, per Cent.	Skin Elasticity	Remarks	Temperature, C.	Remarks
0	3,730	....	....	....	....	36.8	Pelvic abscess
1	.....	37.8	....	Normal	Jaundice	37.1	Endometritis
2	3,410	36.9	5.75	Normal	Jaundice	37.8	
3	3,440	37.2	5.34	Normal	Jaundice	40.5	
4	3,350	38.5	6.97	Normal	Jaundice	41.5	
5	3,300	39.1	6.39	Normal	Weaned	40.5	
6	3,410	36.4	6.86	Normal	Jaundiced	40.0	
7	3,350	36.6	6.34	Normal	Jaundiced	39.0	
8	3,320	36.6	6.28	Normal	Jaundiced	38.5	
9	3,300	37.4	6.62	Normal	Jaundiced	38.5	

Case 8 (Table 2).—*Fever in the Baby Associated with a Febrile Affection in the Mother. No Increase in the Serum Protein Per Cent. Accompanying the Fever. Fall in Temperature on Weaning.*—The mother was a primipara, aged 24. There was no fever until the third day postpartum, when the temperature rose to 40.5 C. (105 F.), remaining at this high level with slight remissions for five days, after which the temperature continued at a lower level. The diagnosis was pelvic abscess, for which the patient was operated on.

The baby weighed 3,730 gm. at birth. His temperature was normal for three days after birth, during which time he lost 390 gm. On the fourth day, one day after the onset of fever in the mother, the baby's temperature rose to 38.5 C. (101.8 F.). It remained elevated until the baby was removed from the breast on the sixth day, after which it was normal for the rest of the baby's stay in the hospital. The serum protein per cent. did not rise above 7 per cent. during the two febrile days. There was no drop in serum proteins when the temperature returned to normal on the sixth day. The skin was normally elastic during the febrile period.

THE TREATMENT OF ACCESSORY NASAL SINUS DISEASE IN CHILDREN [*]

H. B. LEMERE, M.D.
OMAHA

The accessory nasal sinuses in children vary in their relative size and development. Schaeffer's[1] measurements in a series of cases show that the antrum is by far the largest cavity at birth and that it retains this relative size in regard to the other nasal sinuses. In my experience it has been the seat of infection much more frequently than have the other nasal sinuses.

Attention has been drawn to infection of the nasal sinuses in children by one or several of the following symptoms: Profuse nasal or postnasal discharge, cough, persistent mouth breathing after tonsil and adenoid removal (Case 1), pale face and lips, running ear, otitis externa, mastoiditis[2] poor appetite, recurring bronchitis,[3] pneumonia and asthma, (Case 5), pleuritis, headaches, loss of appetite, mental hebitude, chorea and nervousness, arthritis[4] chronic pharyngitis, facial acne, conjunctivitis, both phlyctenular and interstitial keratitis[5] swelling of the cervical lymph nodes.

The diagnosis can be made from:

1. *The Discharge.*—In any case of profuse purulent or mucopurulent discharge from the nose sinus infection will account for the discharge. If the discharge cannot be demonstrated—from the history and from the inspection of the nasal cavities and the posterior pharynx—the post-nasal spray will often expell large quantities of secretion from the nose and throat, or these secretions may be brought into evidence on the administration of ether for tonsil and adenoid operations. Atrophy of the nasal mucosa, with glazed sticky scant secretion, usually indicates a long standing antrum infection with involvement of the bone.

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[*] Received for publication, May 26, 1922.

[*] From the Department of Otology University of Nebraska Medical Department.

1. Schaeffer, J. P.: The Nose and Olfactory Organs, Philadelphia, P. Blakeston Sons Company, 1920.

2. As a routine I have roentgenographed the sinuses in cases of mastoiditis and have usually found an antrum condition present.

3. Mullin, W. V.: Ann. Otol., Rhinol. & Laryngol. **30**:683 (Sept.) 1921.

4. Dean and Byfield: University of Iowa Studies **2**:15 (April 15) 1921.

5. I have found marked opacity of the antra on roentgen-ray examination of syphilitic children suffering from interstitial keratitis.

2. *Signs of General Toxemia.*—The signs of general toxemia are too well known to be enumerated, but when present, infected nasal sinuses should be considered as among the most likely source of the toxin.

3. *The Roentgenogram.*—The roentgen ray is of great value as a diagnostic aid in antrum infections. In children, however, a dense shadow rarely shows, but a slight density greater than is normal has decided diagnostic value. In few of these cases should an operation be performed, and the roentgen-ray findings are mainly valuable in indicating that treatment should be instituted. As the treatment I have outlined is the same no matter which sinus is affected, no particular localization is necessary. The roentgenograms are also useful to show the progress being made as the result of treatment.

4. *Puncture and Irrigation.*—These procedures are useful in institutions but they are impracticable and quite dispensible in office practice.

5. *External Evidence,* such as broadening of the nasal bridge, and a *skin eruption* over the nasal bridge sometimes may be present.

6. *The pharynx* posterior to the tonsils is often fiery red or covered with mucus or has a thickened mucous membrane with enlarged follicles.

As we recognize the prevalence of antrum disease in children, and as we appreciate its far reaching secondary results, we are impressed with the necessity of working out a satisfactory treatment other than operative or one necessitating prolonged hospitalization. As my patients were mostly office patients, the riot which ensued on any attempts to carry out any effective treatment was so appalling that for some time I contented myself with supplying washes and instillations to be used by the parents in the less exciting environment of the home. However, I found these methods to be exceedingly unsatisfactory and unreliable. I then started to train these children to allow me to use the postnasal spray with compressed air. I found that after winning their confidence and applying the spray to their parents as an example of its painlessness, that after two or three sessions I was able to wash out the nasal fossae thoroughly from the postnasal fossa. This I consider the very best way of cleansing the nasal fossae and also of freeing the ostea of the antra. One has only to see it applied to these little ones to realize its efficiency in expelling large quantities of mucopus from the throat and nose.

There is a great advantage of the postnasal spray over douches and anterior nasal syringing in that I have never once seen any of the wash or infected secretion driven into the middle ear through the eustachian tube. Any spray applied through the anterior nares, if it is to be of sufficient force and volume to clear the nasal fossae and pharynx, will cause considerable trauma and bleeding, thus defeating its aim. With the postnasal spray the only bleeding is from the pharynx and this only when adenoids or granulation tissue are present. This bleeding rarely takes place after the first two or three applications and seems to be beneficial in relieving the congestion of the nasopharynx.

The postnasal spray should be applied as frequently a is necessary to keep the head clear and to allay the general symptoms. This application should be made daily in some cases and in others only once or twice a week. The average is every other day for about a month and then less frequently. The procedure is of such a simple nature that an inexpensive apparatus is provided for the parents and they are instructed in its use. This, I think, is the proper solution of the problem in many cases. There are so many of these mild antrum conditions prevailing which demand treatment if the children are to reach their proper development, that rhinologists and pediatrists would be swamped with these patients. The parent has only to see the increased well being resulting from a few weeks of this treatment to be willing to provide the means of continuing the treatment himself at home.

Any good alkaline and antiseptic solution can be used. I have for many years used the following modification of Dobell's solution as a nasal wash: Sodium biborate, sodium bicarbonate, 6 gm. each; phenol, 2.5 c.c.; glycerin, 15 gm.; peppermint water, 100 c.c., and distilled water, sufficient to make 480 c.c. This solution is used freely in an atomizer provided with a No. 56 postnasal tip.

I have used this treatment for the past two years for patients aged from 3 to 18 years. All patients have improved very greatly in that the symptoms and signs were greatly lessened or disappeared entirely for a time. During these periods of remission, the strength and resistance of the child was increased, and on reinfection a few treatments would be sufficient to effect recovery. It is my belief that this treatment will often eradicate the infection in children under 8 years. In children over 8, it is mainly supportive of normal development until the child is sufficiently mature to permit of making a patulous opening from the antrum into the inferior meatus by means of an operation. Only a small percentage of children have the poise to go through with a nasal operation under local anesthesia so that ether will generally be necessary when it is considered advisable to operate. Dean's[6] method is given below.

The exact relationship of the antrum to the inferior meatus is ascertained by a careful roentgen ray study. If the antrum has developed sufficiently low to lie well below the inferior turbinate attachment, the opening is made in the inferior meatus; if the antrum has not descended this far, the opening should be made in the middle meatus. I have found that the opening made in the middle meatus has a tendency to close and that often it is difficult to find it some months after operation. In making the opening from the inferior meatus, the inferior turbinate is turned up out of the way and by means of a bone curet and rasp a sufficiently large opening is made so that later a cannula can be introduced for washing. The inferior turbinate is now turned back to its proper place. If the inferior turbinate covers up the opening so that it would be impossible to introduce a small cannula without pressure, it is advisable to remove a small portion of the anterior end of the bone, as much of the success of after treatment will depend on the possibility of painless washing of the antrum. It must be emphasized to the parent that the operation will not cure the condition but only render the antrum accessible to treatment, and that in order to effect a cure the patient should be under periodic treatment for months and under observation for at least a year.

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[6] Dean and Byfield: University of Iowa Studies **2**:7 (April 15) 1921.

Instillations of solutions of argyrol, 15 per cent.; phenol in glycerin, 2 per cent.; chloramine T in glycerin or 1 per cent.; dichloramine T in chlorcosane, 1 per cent., are useful whether made in the nose after the postnasal spray treatment or injected directly into the antrum as postoperative treatment after the antrum has been opened.

Dean[7] advises the use of suction by means of Haskins' nasal catheters.

The chronic involvement of the sinuses always originates from the lack of complete resolution of an acute infectious disease. It seems, therefore, that under prophylaxis, we should consider especially routine local treatment of the accessory nasal sinuses following the acute exanthemata. The general relief following the recovery from measles, scarlet fever, etc., is so great that little attention is paid to a remaining purulent condition of the nose, and the acute condition is allowed to become subacute or chronic. A few applications of the postnasal spray during the existence of the exanthemata and during convalesence would do much to prevent the development of so many cases of chronic accessory nasal sinus disease.

Many of these cases clear up simply by removal of the adenoids which probably act mechanically by preventing nasal breathing and causing retention of the infected nasal secretions. Dean[8] has found that diseased tonsils will keep active a sinus infection which may disappear on their removal. Parents must be warned, however, that removal of the adenoids and tonsils will not always clear up an existing infection and that the child should be observed for a year after the operation. Many children who are operated on for return of adenoids

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7. Dean and Byfield: University of Iowa Studies **2**:8 (April 15) 1921.
8. Dean and Byfield: University of Iowa Studies **2**:10 (April 15) 1921.

are really suffering from accessory nasal sinus disease and the condition only clears up when treatment is directed to the sinuses.

REPORT OF CASES

Case 1.—M. K., aged 3½ years, was brought to me with a history of catching cold easily, and of doing a great deal of coughing. Her family physician who referred her to me, had advised the removal of adenoids and tonsils.

Examination.—The child was of normal size and weight but was a mouth breather, and coughed a great deal. The skin below the lid was blue in color. The tonsils were greatly hypertrophied. Much mucous secretion came from the nose but the nares were sufficiently patulous for breathing.

Treatment.—The tonsils and adenoids were removed under ether anesthesia. During the operation it was noted that there was profuse secretion from the nose into the throat.

Course.—The cough was relieved to a great extent for three weeks when it returned, keeping the child and parents awake the greater part of the night. A second examination showed that the pharynx was fiery red and that it was thrown into vertical folds on gagging. The nose was partly filled with mucopus. The child was pale, tired, nervous and fretful.

A diagnosis of sinus disease was made. This was verified by roentgen-ray examination. The left antrum was cloudy and the right antrum was slightly cloudy.

Postnasal spraying was commenced and a large quantity of mucus was expelled through the nose. The results were immediate. The child slept through the night for the first time for a week. After the second treatment, the child was entirely tractable and did not cry or resist the spraying. Gradually her appetite became good, her color improved and she went through the rest of the winter without further bronchial trouble.

Case 2.—F. M., aged 13, when seen by the family physician two weeks ago, had a temperature of 102 F., suffering with severe pain in the left cheek. There was a great deal of discharge from the nose, particularly from the left nostril. He had never had an attack like this before, but was always subject to colds. His physician made a diagnosis of antrum infection. This diagnosis was verified by the roentgen ray which showed the right antrum almost closed, the left antrum completely blocked and the other sinuses in a questionable state. The middle turbinates were boggy and swollen. His parents stated that for several months he had not been as robust as formerly, and that he had been subject to bronchial attacks.

Treatment.—After three months of postnasal spraying he regained his normal strength. Another roentgenogram taken at this time showed the right antrum one plus, and the left antrum one and one-half plus. The other sinuses were clear. He had not had any bronchial attacks during the variable weather prevailing through the season he was under treatment. He is apparently in robust health. He should be kept under observation and treatment, when necessary, for the next two or three years as the roentgen ray shows still some latent infection.

Case 3.—S. R., boy, aged 9. His mother states that he has not been well for the past four years. He is listless, has a poor appetite, is pale and somewhat small for his age. His nose discharges summer and winter. Adenoids were removed three years ago.

Examination.—The tonsils were small; pus was expressed fairly easily. Mucopus was dropping from the posterior nares into the nasopharynx in large globules. The teeth were clear. Mucopus was present in both middle fossae of the nose.

Diagnosis.—Nasal sinus disease; mild infection, verified by roentgen ray which showed the right antrum to be cloudy, the left antrum slightly cloudy, and the other sinuses clear.

Treatment.—This consisted in postnasal spraying three times a week at the office and a nasal wash at home. Errors in diet and hygiene were eliminated.

Course.—The boy showed marked improvement from the start and in two months he was a normal healthy boy with red cheeks and a good appetite, and he was doing well in school. At this time it was decided to remove his infected tonsils. The sinus infection is not cured but it is controlled so that he is going on to healthy development.

Case 4.—F. D., boy, aged 7, when first seen was in bed, with a high temperature, fiery red pharynx and mucopus in the nose. The tonsils and adenoids had been removed. The boy had a history of constant poor health, nervousness and repeated colds.

Treatment was given for the acute condition and on recovery roentgen-ray examination showed all sinuses slightly cloudy. The boy was taken out of school, given outdoor life and supportive treatment, and treated regularly with the postnasal spray at the office.

His general health became normal and he went through the winter without colds and with a steady gain. His family left this city and instruction was given to continue the treatment as the local condition was under control but not cured.

Case 5.—R. E., boy, aged 7, has had asthma for two years. The attacks last longer than formerly but they are less severe. His tonsils and adenoids were removed one year ago, but he did not get much relief.

Mucopus was present in nose and nasopharynx. The bases of the tonsils remain. A roentgenogram taken four months previously showed both antra cloudy; the other sinuses were clear. The child is pale and nervous.

Treatment.—As the parents lived at some distance and the asthma was becoming established, and was of long standing, it was considered better to make an opening beneath the inferior turbinates according to Dean's method. The remains of the tonsils were removed, and some adenoid bands were broken up. The parents were instructed in the use of the postnasal spray and before the child returned to his home he was trained to submit to treatment.

Course.—He went through the winter without any asthma, gained in weight and has good color. There is still mucopus in his nose and throat occasionally and at times he needs the postnasal spray. It is too early yet to say that the asthma may not return but the effect of the operation and treatment have been so far successful.

The study of sinus disease in children only dates back a few years and our ideas on all phases of this important subject have yet to be crystalized. It is with the purpose of arousing interest and further observations by others that I have submitted this brief paper.

A NEW ERUPTIVE FEVER ASSOCIATED WITH STOMATITIS AND OPHTHALMIA

REPORT OF TWO CASES IN CHILDREN *

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During a period of three months we had the opportunity of observing two cases of an extraordinary, generalized, eruption with continued fever, inflamed buccal mucosa and severe purulent conjunctivitis. The first patient was seen on the tenth day of illness and followed to recovery. The second patient did not come under observation until the twenty-second day after onset of the illness; but the skin lesions at that time corresponded exactly with those of the first case at the same stage of the disease, and a careful description of the eruption as seen in the first week establishes its identity with that in Case 1.

The condition was so unusual and so entirely unlike anything previously observed, that pains were taken to get as many expert opinions as possible from men of wide clinical experience. At the same time, a search was made in the literature of eruptive fevers and allied dermatologic conditions. No diagnosis could be made to correspond with the symptoms and course of the eruption in these two cases and no description was found of a skin condition in any degree comparable.

Figures 1, 3, 4 and 5 will make clear, as verbal description cannot, the nature of the eruption in its several phases. Figure 1 shows the boy on the thirteenth day of his illness. The eyes are swollen shut, exuding pus; the lips are black with crusted blood. The eruption is complete, except for the feet and hands, while on the shoulders, scaling of the horny crusts is already in progress. Figure 3 shows the same boy on the twenty-fourth day. Many of the lesions on the back and chest have already crusted and dropped off; the later lesions of the feet and hands show clearly, but on the arms and thighs there is an exaggerated effect of confluent desquamation due to the liberal use of bland ointments and powder on the skin. In this detail the photograph is somewhat deceptive. Figure 4 shows the same boy on the thirty-third day of his illness. The mouth and eyes are normal; the face, chest and back are practically clear, except for pigmented spots which mark the site of lesions which have crusted and fallen away. Figure 5 shows the other boy (Case 2) eleven weeks after the onset of his disease.

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* From the Department of Diseases of Children, Columbia University and the Children's Medical Division, Bellevue Hospital.

The sunken, sightless eyes bear witness to the destructive effect of the ophthalmia in this case. Over the whole body may be seen the brownish pink pigmented spots that mark the position of the eruption.

In the uncertainty of diagnosis, each case was treated in isolation with the strong impression in the minds of all that this disease, with its high temperature and profuse eruption, should be considered in the group of infectious, eruptive fevers. There was an interval of a litttle more than a month between the arrival of the patients at Bellevue Hospital and no possible contact could be traced between the families—living, as they were, in widely separated sections of the city. At any rate, no other cases developed; and while the presumption remains that this condition is an infection, there is nothing to indicate that it is spread by immediate contagion.

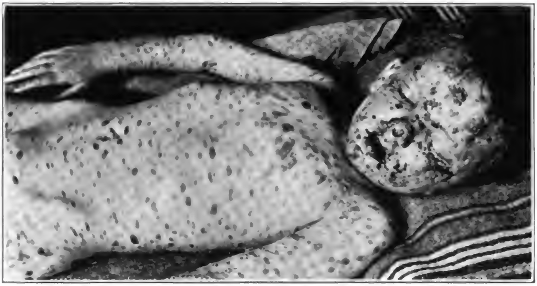

Fig. 1.—Case 1. Nature and extent of eruption on the thirteenth day of the illness.

REPORT OF CASES

Case 1.—*History*.—H. S., a white boy, aged 8 years, was admitted to the children's service of Bellevue Hospital, May 1, 1922, on the tenth day of his illness. There was nothing significant in the family history; he had diphtheria at 18 months, pertussis at 3 years and measles at 7 years. He had been successfully vaccinated and the tonsils had been removed at 7½ years. His general health had been good until shortly following the tonsillectomy when he was in a hospital for fourteen weeks with a septic temperature, enlarged spleen, jaundice and a blood culture which showed *Staphylococcus aureus* on two occasions. He recovered from this, and was apparently well for two and a half months prior to the onset of the present illness.

Onset of Illness.—Ten days before admission, he complained of a mild sore throat and general malaise. He was not very sick at first, but felt weak and went to bed. The next day he complained of pain in the eyes and did not want to eat because his mouth hurt him. Soon pus was seen running from the inflamed eyes and on the third day reddish spots were noticed on the back of the neck. The body was not examined until the seventh day when the skin was found to be covered with reddish brown spots; only a few such spots were noted on the face, legs and arms. While at home, the temperature was not taken.

Physical Examination.—On admission the boy was acutely ill with a temperature of 103 F. He was well nourished, mentally clear and cooperative, but was prostrated and unable to open his swollen eyes. The lids of both eyes were edematous and thick pus streamed down the face from the palpebral fissures. There was marked blepharitis marginalis, chemosis and inflammation of the bulbar conjunctiva with haziness of the left cornea. The lips were cracked, bleeding and encrusted. The tongue was swollen, bright red and fissured, and the mucous membrane of the mouth was inflamed with small bullous lesions which rapidly broke down, leaving a raw and angry surface. The scalp was quite free of any eruption but the face showed large blotches of dried pus, considered secondary to the purulent discharge from the eyes spreading over the papular lesions of the cheeks and forehead.

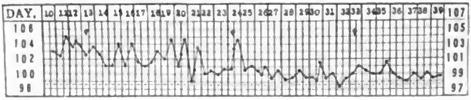

Fig. 2.—Temperature chart of Case 1. P marks the days when photographs were taken.

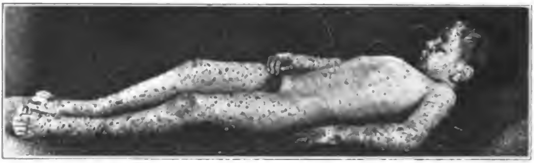

Fig. 3.—Case 1. Twenty-fourth day of the illness.

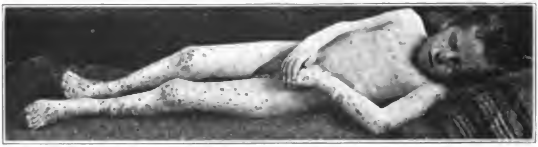

Fig. 4.—Case 1. Thirty-third day of the illness.

The trunk, arms and thighs were thickly set with discrete, oval, brownish purple papular lesions, varying in size from 0.5 to 2 cm. in the longest diameter. A few of the largest spots showed a yellowish, dry, necrotic center. There was no vesicle, nor pustule formation; no induration about the papule; no areola and the skin between the lesions seemed to be perfectly normal. The forearms and legs showed what seemed to be the more recent lesions. These were less raised, of brownish red color, paling somewhat on pressure, and more closely set than were those of the trunk and thighs (Fig. 1).

Careful physical examination disclosed a faint short systolic heart murmur, heard best to the left of the apex and not transmitted. The spleen was palpable 4 cm. below the ribs, and the liver edge could be felt a finger's breadth below the costal margin. Otherwise, there were only normal findings.

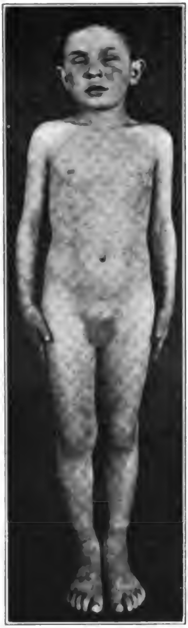

Fig. 5.—Case 2. Eleven weeks after onset of illness. Recovery was complete except for total blindness. Persistent pigmentation shows at the sites of the skin eruption.

Laboratory Examination.—Cultures made from the eyes and throat showed a mixed infection of common cocci and bacilli with no predominating organism and no gonococci. From the necrotic center of one large papule a pure strain of *Staphylococcus aureus* was grown. The blood culture was sterile. The Wassermann reaction was negative.

Blood: The blood count showed 4,000,000 red blood cells with 75 per cent. hemoglobin, and 10,000 leukocytes with 82 per cent. polymorphonuclears and 18 per cent. lymphocytes and transitionals. The blood chemistry was also done and all values were determined to be within the normal range.

Urine: Except for a trace of albumin, which was a constant finding during the period of high temperature, the urine was negative.

Course.—For the next eleven days (from the tenth to the twenty-first day of the illness) the temperature ranged between 101 and 105 F., with a fall to the 100 degree level after the twenty-fourth day (Fig. 2). At each examination the blood showed a definite leukopenia.

During this time there was no complaint of pain or itching or discomfort in the skin lesions. Photophobia and pain in the eyes persisted, but the edema of the eyelids and the purulent discharge yielded to treatment with warm boric acid instillations, dilatation of the pupils with 1 per cent. atropin and the application of 1:5,000 mercuric chlorid in petrolatum twice daily. The right eye cleared rapidly, but the left cornea was already ulcerated and it healed very slowly, with resultant scarring of its lower segment.

New lesions were seen to appear on the skin of the forearms and legs, the palms and soles, for the first week after admission, but none after the eighteenth day since onset. These were at first pale and macular, rapidly becoming firm, dry, purplish papules like those seen on the trunk at the time of admission. Meanwhile, the earliest skin lesions had begun to resolve into horny, flattened, thick scales, with raised, papery edges. At this stage the fever dropped to its lowest level (Fig. 3).

Blood Examination in Case 1

	19th Day	26th Day	37th Day
Leukocytes	4,600	6,700	8,700
Polymorphonuclears	62	52	58
Small lymphocytes	33	45	40
Large mononuclears	3	0	0
Eosinophils	0	2	2

As the resolution advanced in the same order as the appearance of the lesions, these dry horny scales dropped off from the neck and back, then from the chest and abdomen and thighs, and last of all from the arms and legs, leaving a dull reddish area of apparently normal skin to mark the site of the lesions. There was no instance of pitting or scarring of the skin (Fig. 4).

The inflammation of the mucous membrane of the mouth, lips and tongue subsided within a week of admission. This did not interfere with the taking of nourishment and no gastro-intestinal symptoms were present at any time.

The subsequent history of this case is not especially significant. After a period of normal temperature for two weeks a left otitis media developed; this went on slowly to a mastoiditis for which the boy was operated on June 22. At this time a few crusts still remained on the forearms and feet.

Case 2.—*History.*—S. M., was a Jewish boy, aged 7 years, with a negative family history, who had been always strong and well except for measles at 4 years. He had been vaccinated successfully.

Onset of Illness.—Three weeks before admission, he complained of pain in the eyes and weakness. The next day the eyes were discharging, and a rash was noted on the body which the family physician called "black measles." On the third day of his illness he was taken to the Willard Parker Hospital, where he was found to have a temperature of 103 F., with signs of bronchopneumonia at the right base, a purulent conjunctivitis with great edema of the lids, and a skin eruption of which the tentative diagnosis of erythema multiforme was made. This eruption was described on the third day as being macular, hemorrhagic, with a few papules, with areas of excoriation on the face.

The eyelids were edematous and pasted shut with thick pus, and the mucous membrane of the mouth was practically exfoliated. The boy remained at Willard Parker Hospital for two and a half weeks, with the pneumonia resolving gradually. The temperature ranged from 101 to 104 F. for two weeks, then became irregular at a lower average with an occasional rise to 103 F. The boy was irrational during the first week, and there was great prostration, weakness and loss of flesh. In spite of instillations of boric acid solution and argyrol, corneal ulcers formed, with perforation and abscess formation in both eyes involving all the structures of the globe.

Simple ointments were applied to the skin lesions, which crusted and dropped off the chest and back by the end of the third week.

He was transferred to the Children's Service of Bellevue Hospital on the twenty-second day of his illness, March 11, 1922.

Physical Examination.—On admission the boy was acutely ill, much wasted, with a temperature of 102 F., mentally clear, but totally blind. The lungs showed signs of a resolving pneumonia of the right lower lobe. The eyes were the seat of a panophthalmitis, with destruction of the cornea and lens. Pus was still oozing from the granulating tissue of the shrunken eyeballs.

The skin of the trunk was the seat of irregularly oval pigmentation of a reddish brown color, rather evenly distributed except below the nipples where there were confluent areas. This skin was quite normal in appearance, except for the pigment, and showed no trace of scar tissue.

The arms and legs showed oval brownish red horny crusts, varying from 1 to 2 cm. in the longest diameter without areola or surrounding induration, and without trace of exudate or pustule formation. There was no complaint of pain or itching. Otherwise the examination was quite negative.

Course.—The lung condition cleared slowly with a temperature varying between 101 and 103 F., for a week, then falling to the 100 degree level for eight days. The eyeballs healed by granulation. The skin condition resolved progressively by the falling off of the thick oval horny crusts from the thighs and arms, and, last of all from the feet and soles, each crust leaving to mark its site an area of reddish brown pigment. These areas were identical with the marks found on the back and chest at time of admission.

The family refused to allow blood to be taken for a Wassermann test and insisted on removing him from the hospital fifteen days after admission. Later, this boy was visited in his home and found to be in excellent condition except, of course, for his blindness. With some difficulty consent was obtained for a photograph (Fig. 5).

SUMMARY

1. Two cases have been observed of a generalized cutaneous eruption, not conforming to any recognized dermatologic condition.

2. Both cases occurred in boys, one aged 7, the other 8, coming from widely separated parts of New York City, with no possibility of contact.

3. Both cases manifested a purulent conjunctivitis, in Case 2 going on to panophthalmitis and total loss of vision, and in Case 1 responding to treatment, but leaving a severe corneal scar. The pus showed pyogenic organisms only; no gonococci.

4. A high and continuous fever was present in both cases, explainable in Case 2 by a lobar pneumonia, but in Case 1 without apparent cause other than the skin condition.

5. The eruption showed certain characteristics, identical in each case. The onset was with fever, the rash appearing on the back of the neck

and chest, spreading to the face, arms and legs during a period of about eighteen days, the last lesions to appear being on the soles and palms. At this time resolution of the first lesions began.

The eruption consisted of oval, dark red to purplish macules, separated by normal areas of skin. These became in a few days raised firm papules of brownish purple, from 0.5 to 2 cm. in the longest diameter, without areola, and without subjective symptoms of pain or itching at any time. A few of the largest spots showed a yellow, dry, necrotic center. The lesions on the forearms and shins were smaller and more thickly crowded together. No pustules or vesicles were to be seen. The scalp was at all times free of lesions; but the mouth and lips were intensely sore and inflamed. In Case 1 bullae were noted in the mouth at the end of the first week.

After the third week resolution began in the order of appearance of the lesions. This consisted of a shrinking of the macule to a horny oval of dark brown color, with raised papery edges. From the fourth week these scales dropped off, leaving a faint pigmented area, without pitting or scarring. By the fifth week the chest, face and back were clear, except for pigmentation, while resolution and crusting were still going on on the forearms and legs. Fall of temperature coincided with the period of resolution of the skin lesions.

DIAGNOSIS

1. A skin eruption from drug ingestion is ruled out by careful inquiry which showed that no drugs whatever had been administered in either case.

2. A skin eruption from food poisoning can hardly be considered from the entire absence of gastro-intestinal symptoms in the presence of a high and sustained temperature reaction.

3. Syphilis is to be excluded by the character of the lesions, the age of the children, the negative history, and the negative Wassermann reaction in Case 1.

4. Pemphigus was suggested, from the observation of bullae in the mouth in Case 1. Nothing further in the course of the disease, the appearance of the eruption and its evolution gave any support to this diagnosis.

5. Hemorrhagic measles, as it happened, was the primary diagnosis of the family physician in each instance. Both children had already had measles, in Case 1 at 7 years, and in Case 2 at 4 years. While excusable at the onset, this diagnosis is quite indefensible in view of the distinctive character of the lesion as described.

6. A sepsis with generalized eruption must be considered as a possibility, in spite of the negative blood culture in Case 1. This diagnosis

is suggested by the history of a prior sepsis in Case 1 and might account for the temperature and course and the occurrence of a pneumonia in Case 2. The superficial nature of the lesions, their character and progressive appearance over nearly three weeks and the lukopenia argue against this supposition.

7. Erythema multiforme, from some unknown toxic cause, was proposed as a diagnosis, but this is unsatisfactory from the character and distribution of the lesions, the lack of subjective symptoms, the prolonged high fever, and the terminal heavy crusting.

8. There remains the possibility that this condition represents a distinct disease which has not hitherto been recognized.

Comment.—While the true diagnosis of this condition must be left an open question, the report of these two cases seems justified if only to draw attention to the serious effects to be expected unless the eyes in any similar case receive early and painstaking treatment. The boy in Case 2 is totally blind, while the other boy only escapes with an impairment of vision in one eye. Furthermore, it is hoped that this report may lead to the study of other or similar cases. Quite possibly the observation of this condition in its first stages may clear up the vexed question of its etiology.

Finally, we have been impressed by the striking picture presented by these cases. Here is a syndrome of dramatic onset, with fever, conjunctivitis and cutaneous eruption. The child is prostrated, the mouth and tongue are inflamed and raw, the eyelids are swollen and pus streams from the eyes. There is a course of three or more weeks of high fever, with leukopenia. The eruption, unlike any hitherto described, comes out progressively, for two weeks or more, matures and resolves in horny crusts, in the order of its appearance. The temperature falls with this resolution of the skin lesions. This syndrome suggests strongly an infectious disease of unknown etiology. We believe that this condition deserves to be considered a definite clinical entity.

We wish to express our appreciation of the kindness of Dr. L. Emmett Holt, Dr. John A. Fordyce and Dr. Warfield T. Longcope, who saw one or both of these cases in consultation.

CONGENITAL DUODENAL OBSTRUCTION: MALROTATION OF THE INTESTINE

REPORT OF CASE *

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In this report the clinical rather than the developmental aspects of congenital duodenal obstruction will be emphasized. It seems that enough cases have been recorded to warrant giving a more definite clinical picture, and this may serve to center interest in them as clinical cases rather than as pathologic specimens. Unfortunately, the first few days of life are a veritable shadowland for diagnosis and treatment. The infant that seems barely holding on to life may be a thriving youngster a few days later, and, on the other hand, sudden and unexplained exitus of a baby apparently not very ill is an all too frequent occurrence. Similarly, at this time of life exploratory laparotomy is an adventure. It is, therefore, with some hesitancy that the effort is made to group the striking clinical features of congenital duodenal obstruction and to suggest that at least some of the cases may be brought within the reach of surgical assistance. Perusal of the literature, in addition to the study of a single case, forms the background for the discussion and conclusions.

From the clinical standpoint, the possible duration of life of infants suffering from duodenal obstruction is of first importance. As far as this is related to the anatomic anomaly, the duration of life is dependent on whether there is atresia (complete occlusion of the intestinal tract) or merely stenosis (partial obstruction). Of thirteen cases of stenosis collected by Kreuter in 1905, four patients lived for a week or more.[1] A search of the literature since 1905, probably not complete, of cases of partial obstruction in which the patients live more than a week, has revealed an even greater number.[2] Four infants died during the second week of life, and three during the second month; four others lived from four to nine months, one for twelve months,

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* From the Pediatric Service of the New York Nursery and Child's Hospital and the Pediatric Department of Cornell University Medical School.

[1] Two infants lived seven days, one lived twelve days and one six months.

[2] This refers only to infancy and not to those cases of obstruction discovered in later life, due to bands, anomalous peritoneal fossae, malrotations, etc.

one for eighteen months and one for two years.[3] The mere duration of life is emphasized because it indicates that in some cases there is at least time for surgical intervention.

Efforts at treatment have been made. Colwell, in 1912 recorded five cases in which enterostomy had been done, although unsuccessfully. Commenting on the reports of Keith and Buchanan of infants living nine and eighteen months, he remarked, "it would seem that cases should be subjected to laparotomy, and, if possible, gastro-enterostomy should be performed." Indeed, since then such an operation has been done successfully. Ernst, in 1916,[4] operated on an infant 11 days old. There was an obstruction "at the upper side of the transverse mesocolon" and Ernst performed a duodeno-entero anterior anastomosis. Eleven months later the child was a "vigorous well developed youngster."

The symptomatology of cases living more than a week depends on the location and degree of obstruction. When the obstruction is situated below the ampulla of Vater, the vomitus is bile stained. This is emphasized by nearly all the authors who considered the symptomatology of the cases they reported.[5] Bradford believes that "vomiting occurs after the lapse of a longer period following feedings than does the vomiting caused by stenosis higher in the tract." In nearly all cases there was difficulty in excluding pyloric stenosis, and in many cases that was the diagnosis made. Tumor was mentioned by only a few authors; it was a vague sign.[6] Peristaltic waves were more frequently found. Fecal stools, the occurrence of the residue of milk digestion or the continuance of meconium stools beyond the usual period were helpful in determining partial or complete obstruction. Prolongation of life, despite an almost complete obstruction was a surprising

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3. Commandeur: Lyon méd. **114**:423, 1908. Freeman, R. G.: Arch. Pediat. **27**:37, 1910. Shaw, H. L., and Baldauf, L. K.: Tr. Am. Pediat. Assn., 1907, p. 36. Weber: München. med. Wchnschr. **60**:212, 1913. McClanahan, H. M.: Arch. Pediat. **25**:533, 1918. Stolte, K.: Monatschr. f. Kinderh. **12**:341, 1913. Colwell, E. M.: Quart. J. Med. **5**:401, 1911. Spriggs, N. I.: Guy's Hosp. Rep. **66**:143, 1912. Van Der Bogert: Arch. Pediat. **33**:194, 1916. Schroder, C. H.: J. A. M. A. **78**:1039 (April 8) 1922. Cautley, E.: Brit. J. Child. Dis. **16**:184, 1919. Bradford, O. F.: J. Missouri M. A. **15**:307, 1918. The case of Helmholz and Little (Johns Hopkins Hosp. Bull. **16**:231, 1905) should be included, although it was a complete obstruction. A gastro-enterostomy was done and the child lived eight days.

4. Ernest, N. P.: Brit. M. J. **1**:644, 1916.

5. A possible exception to this statement is Van Der Bogert's case. In an infant, 4½ months old, with a duodenal obstruction 2½ inches from the pylorus "there was no appearance of bile in the vomitus, although unfortunately no chemical tests were made."

6. Loc. cit. Cautley and also Schroder.

feature. In Cautley's case, in which the child lived twelve months "the second part of the duodenum was extremely stenosed, merely admitting the passage of a probe." And Spriggs, performing a necropsy on an infant 9 months old, found a diaphragm occluding the lumen of the duodenum; and, as he remarked, although there was "no evidence of an orifice in this diaphragm, the history of the case proves that some opening must have existed." The uncertainties of abdominal diagnosis, in general, at this early age, combined with variations depending on the position and degree of obstruction, make it very difficult to outline a clear cut clinical picture. One might be tempted to offer a crude rule of thumb, that a symptom complex suggesting but not typical of pyloric stenosis or pylorospasm, in a desperately sick infant, should raise the question of an obstruction in the upper part of the small intestine.

The etiology of duodenal obstruction has been fully reviewed.[7] Many of the anomalies and the theories to explain them are referable to conditions within the lumen of the intestine, valves, folds of mucous membrane, failure of absorption of embryonic epithelial plugs, etc. The case to be reported was not studied from that angle, and although it is extremely unlikely, such a factor might have been operative in addition to malrotation.

REPORT OF CASE

History. — Baby R. was born on the obstetric service of the New York Nursery and Child's Hospital, Dec. 24, 1920. Toxemia of pregnancy necessitated delivery by cesarean section during the eighth month of parturition. The premature baby weighed 6½ pounds and appeared well developed. When 7 days old the child was transferred to the pediatric service with the history of 1½ pounds loss of weight and vomiting of all food since birth; the vomitus was dark green in color and not projectile.

Course.—Dr. Anderson, the resident physician, noted that the baby was emaciated, the fontanel slightly depressed, the abdomen sunken and the liver and spleen palpable. The infant lived twenty-six days after admission to the pediatric service. Although occasional days passed without vomiting, persistent bilious vomiting was the striking symptom. Lavage on numerous occasions also revealed bile stained fluid, at times as much as from 3 to 4 ounces of "thick pea soup material." At first, the stools were yellow and indicated the passage of food through the intestines; toward the end they became watery and green. The roentgen-ray examination was not conclusive. It showed no peristaltic waves, an atonic stomach and a threadlike shadow outlining the course of the duodenum. Three days before death, definite peristaltic waves were seen. No tumor could be felt. Atropin was administered for a few days. It is hardly necessary to detail the supportive measures employed—saline solution subcutaneously and into the peritoneal cavity, and transfusion—and the care in matters of feeding.

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[7] Kreuter, E.: Die Angeborenen Verengerungen u. Verschliessungen des Darmkanals. 1905, St. George, A. V.: Am. J. Dis. Child. **15**:354 (May) 1918, and Cordes, L.: Arch. Pediat. **13**:401, 1901, in addition to those of Spriggs, Cautley, and Helmholz and Little. These refer to atresia as well as to stenosis.

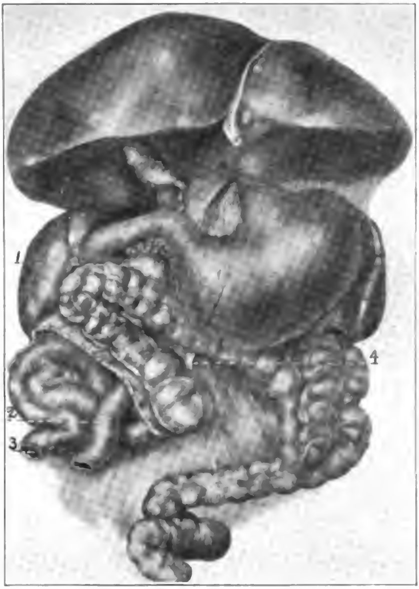

Fig. 1.—The liver has been pulled upward and the transverse colon downward. This gives the impression that pressure occurred lower down in the duodenojejunum than was actually the case. (1) Sharp duodenojejunal angle; (2) jejunum; (3) lower part of ileum; (4) band attaching cecum to posterior abdominal wall.

Diagnosis.—The diagnosis lay between pyloric stenosis and obstruction below the ampulla of Vater. Bilious vomiting, pointing to relaxation of the pyloric sphincter, was the striking symptom and most of those who examined the infant favored the diagnosis of obstruction. A second transfusion preliminary to exploratory laparotomy was planned when the infant died.

Report of Necropsy.—Aside from the intestinal tract, the necropsy is not of interest. The small intestine occupied the entire right half of the abdomen. The cecum was situated to the left of the midline beneath the transverse colon (Fig. 1). Drawing the cecum downward and to the right, brought out a firm, rather tough band, attaching the cecum to the posterior abdominal wall. The ileum entered the cecum from right to left. The stomach was much dilated and the pylorus was wide and flabby. The dilatation of the first portion of the duodenum was even more pronounced than is indicated in the sketch.[8] The third portion of the duodenum, instead of curving gradually upward, turned to the left, creating a sharp duodenojejunal angle. To express these relations differently, the third part of the duodenum was missing and the duodenojejunal angle was formed by the transverse or second part of the duodenum and the continuous loop of the intestine. As this loop of intestine continued downward, it emerged, clamped between the last few inches of the ileum dorsally and the cecum and ascending colon ventrally. One may picture the ileum and the ascending colon as the blades of a scissors (Fig. 2). The posterior or dorsal blade is formed by the ileum, the anterior or ventral blade by the ascending colon, the ileo-caecal region forms their point of attachment and the duodenum is clamped between them. Figure 2 shows the ascending colon cut and rolled back, uncovering the duodenum as it crosses the ileum. Thus, three factors contributed to the production of the obstruction: (1) the sharp duodenojejunal angle; (2) the squeezing of the jejunum between ileum and colon;

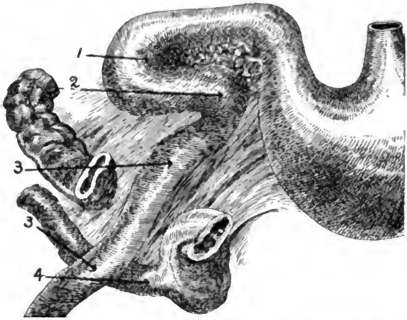

Fig. 2.—Ascending colon cut and pulled back to show mechanism of obstruction. (1) Dilated duodenum; (2) duodenojejunal angle; (3) jejunum; (4) ileum.

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[8] The sketch was made from the preserved and somewhat shrunken specimen.

(3) the binding down of the cecum to the posterior abdominal wall. The fixation of the cecum prevented free mobility, and a freely movable cecum might have exerted less pressure on the small intestine.

It is simpler to describe the anatomic conditions determining the obstruction than to trace their pathogenesis. The explanation of the mechanism of obstruction rests on the determination of the primary factor in the malrotation of the cecum and ascending colon. It will be recalled that in early fetal life the alimentary canal is a vertical tube. As development proceeds, the colon, which is at first on the left side, rotates about the mesenteric axis and the cecum passes across the duodenum and finally descends to the right iliac fossa. "This rotation may be arrested temporarily or permanently in any position during its circuit."[9] In the case presented there are two possibilities. First, there might have been a localized peritonitis that produced a fibrous band maintaining the cecum in the position characteristic of an earlier period of fetal life, that is, to the left of the median line (Fig. 1). According to this explanation, the fibrous band, or rather the inflammation responsible for it, would be considered the primary factor preventing normal rotation of the large intestine. Or, secondly, there might have been some other unknown primary factor interfering with normal rotation; according to this assumption, the fibrous band would be considered the result of a secondary contraction of a loose peritoneal fold. The sharp duodenojejunal angle was surely secondary; most probably it was due to the drag exerted by the small intestine. The loops of intestine hung from the mesentery as from a pedicle instead of spreading out fan shaped in the normal fashion. In either case failure of the intestine to rotate completely was the immediate cause of obstruction since it left the cecum in such a position that pressure upon the duodenum was unavoidable.

DISCUSSION AND CONCLUSIONS

Duodenal obstruction in infants, and especially in new-born babies, embraces too many variant factors to warrant generalizations. The most that can be expected, as far as diagnosis is concerned, is the determination of the presence of obstruction, whether it is partial or complete, and its approximate location. Recording the symptomatology may develop a clearer clinical picture. The results of surgical intervention depend chiefly on the complexity of the lesions. Surgeons who have seen the specimen doubt very much whether anything could have been done in the case described. In general, gastro-enterostomy is the operation indicated. The duration of life in some infants with duodenal obstruction and the successful performance of gastro-enterostomy by Ernst suggest that under favorable circumstances some cases may be amenable to surgical treatment. The cause of the obstruction in the case reported was malrotation of the intestine; whether the malrotation was primary or due to a fibrous band binding the cecum to the left abdominal wall, is controversial.

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[9] Mayo, C. H.: Med. Rec. **81**:401, 1912.

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